Serial No. 08/993,696
Reference 43 of 61


PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61F 2/14

A1

(11) International Publication Number: WO 97/28759

(43) International Publication Date: 14 August 1997 (14.08.97)

(21) International Application Number: PCT/US97/01411

(22) International Filing Date: 7 February 1997 (07.02.97)

(30) Priority Data:
08/599,014 9 February 1996 (09.02.96) US

(60) Parent Application or Grant
(63) Related by Continuation
US 08/599,014 (CIP)
Filed on 9 February 1996 (09.02.96)



(71) Applicant *(for all designated States except US)*: KERA VISION, INC. [US/US]; 48630 Milmont Drive, Fremont, CA 94538-7353 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: SILVESTRINI, Thomas, A. [US/US]; 1701 Las Trampas Road, Alamo, CA 94507 (US).

(74) Agents: CIOTTI, Thomas, E. et al.; Morrison & Foerster L.L.P., 755 Page Mill Road, Palo Alto, CA 94304-1018 (US).



(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

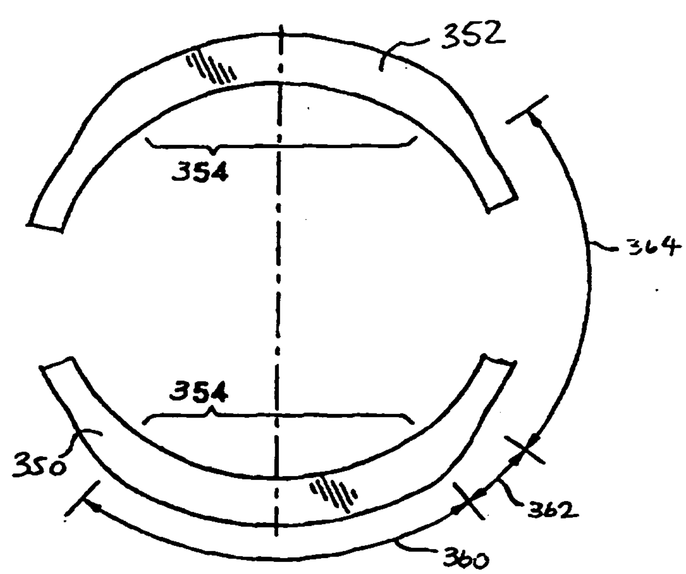
**Published**
*With international search report.*
*Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.*




(54) Title: SEGMENTED INTRASTROMAL CORNEAL INSERT FOR ALTERING CORNEAL REFRACTIVE PROPERTIES AND METHODS THEREOF


(57) Abstract

An intrastromal corneal insert for effecting a change in the corneal curvature to treat conditions such as astigmatism, myopia, and hyperopia. The insert includes one or more arcuate or arc-shaped segments. The extent of corneal correction by such a segment, for a given cross-sectional configuration, is a function of one or more predefined parameters, including the arc angle, radius of curvature, cone angle, modulus of elasticity, and thickness of the segment. The invention also provides for various methods for changing the refractive characteristics of an eye. Generally, the methods involve determining the amount of corrective refraction desired, providing an intrastromal channel which traverses at least a portion of the circumcorneal rotation, and introducing one or more of the inventive segmented inserts.

### *FOR THE PURPOSES OF INFORMATION ONLY*

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

| | | | | | |
|---|---|---|---|---|---|
| AM | Armenia | GB | United Kingdom | MW | Malawi |
| AT | Austria | GE | Georgia | MX | Mexico |
| AU | Australia | GN | Guinea | NE | Niger |
| BB | Barbados | GR | Greece | NL | Netherlands |
| BE | Belgium | HU | Hungary | NO | Norway |
| BF | Burkina Faso | IE | Ireland | NZ | New Zealand |
| BG | Bulgaria | IT | Italy | PL | Poland |
| BJ | Benin | JP | Japan | PT | Portugal |
| BR | Brazil | KE | Kenya | RO | Romania |
| BY | Belarus | KG | Kyrgystan | RU | Russian Federation |
| CA | Canada | KP | Democratic People's Republic of Korea | SD | Sudan |
| CF | Central African Republic | | | SE | Sweden |
| CG | Congo | KR | Republic of Korea | SG | Singapore |
| CH | Switzerland | KZ | Kazakhstan | SI | Slovenia |
| CI | Côte d'Ivoire | LI | Liechtenstein | SK | Slovakia |
| CM | Cameroon | LK | Sri Lanka | SN | Senegal |
| CN | China | LR | Liberia | SZ | Swaziland |
| CS | Czechoslovakia | LT | Lithuania | TD | Chad |
| CZ | Czech Republic | LU | Luxembourg | TG | Togo |
| DE | Germany | LV | Latvia | TJ | Tajikistan |
| DK | Denmark | MC | Monaco | TT | Trinidad and Tobago |
| EE | Estonia | MD | Republic of Moldova | UA | Ukraine |
| ES | Spain | MG | Madagascar | UG | Uganda |
| FI | Finland | ML | Mali | US | United States of America |
| FR | France | MN | Mongolia | UZ | Uzbekistan |
| GA | Gabon | MR | Mauritania | VN | Viet Nam |

# SEGMENTED INTRASTROMAL CORNEAL INSERT FOR ALTERING CORNEAL REFRACTIVE PROPERTIES AND METHODS THEREOF

## Technical Field

The present invention relates to intrastromal corneal inserts and methods for altering refractive properties, including the corneal curvature and/or the aspheric shape, of the cornea of an eye. More specifically, the invention involves intrastromal corneal segments having various predefined parameters, including but not limited to arc angle, radius of curvature, cone angle, thickness, and width, which effect this change when the segments are inserted into the cornea. The invention also involves methods for inserting one or more of the segments into the cornea of the eye.

## Background of the Invention

Anomalies in the overall shape of the eye can cause visual disorders. Hyperopia ("farsightedness") occurs when the front-to-back distance in the eyeball is too short. In such a case, parallel rays originating greater than 20 feet from the eye focus behind the retina. In contrast, when the front-to-back distance of eyeball is too long, myopia ("nearsightedness") occurs and the focus of parallel rays entering the eye occurs in front of the retina. Astigmatism is a condition which occurs when the parallel rays of light do not focus to a single point within the eye, but rather have a variable focus due to the fact that the cornea refracts light in a different meridian at different distances. Some degree of astigmatism is normal, but where it is pronounced, the astigmatism must be corrected.

Hyperopia, myopia, and astigmatism are usually corrected by glasses or contact lenses. Surgical methods for the correction of such disorders are known. Such methods include radial keratotomy (see, *e.g.*, U.S. Patents Nos. 4,815,463 and 4,688,570) and laser corneal ablation (see, *e.g.*, U.S. Patent No. 4,941,093).

Another method for correcting those disorders is through the implantation of polymeric rings in the eye's corneal stroma to change the curvature of the cornea. Previous work involving the implantation of polymethylmethacrylate (PMMA) rings, allograft corneal tissue, and hydrogels is well documented. One of the ring devices involves a split ring design which is inserted into a channel previously dissected in the stromal layer of the cornea. A minimally invasive incision is used both for producing the channel and for inserting the implant. See, for instance, the use of PMMA intrastromal rings in U.S.

Patents Nos. 4,452,235 to Reynolds; 4,671,276 to Reynolds; 4,766,895 to Reynolds; and 4,961,744 to Kilmer *et al.*

Adjustment of intracorneal rings to obtain the necessary correction of the eye normally typically involves an adjustment of ring size or diameter. For example, U.S. Patent No. 4,452,235 describes a method and an apparatus for corneal curvature adjustment by means of adjusting the diameter of the ring. The method involves inserting one end of a split end adjusting ring into the cornea of the eye and moving the ring in a circular path until its ends meet. The ends are thereafter adjusted relative to each other until the shape of the eye has assumed a desired curvature whereupon the ends are fixedly attached to maintain the desired curvature of the cornea.

Another manner in which intracorneal rings are adjusted for selectively correcting abnormalities of the eye involves varying the thickness of the rings. U.S. Patent No. 5,318,047 discloses a method that allows for the refractive correction of the eye by determining the amount of correction necessary, selecting an intrastromal corneal ring of appropriate thickness to obtain the necessary correction from a selection of rings of varying thickness, and inserting the ring into the corneal stroma.

U.S. Patent No. 5,405,384 also discloses an intrastromal intracorneal rings having varying thicknesses for the purpose of creating astigmatism. These rings have at least one region, and often have two or more regions, in which the cross section is thicker or the bulk of the region is more pronounced. By proper alignment of the larger regions of the ring with the eye's anomalies, the astigmatism can be alleviated.

Prior art intracorneal ring implants require forming a continuous circumferential channel within the stroma of the cornea, and thereafter inserting a continuous circular device therein. Such a requirement has important drawbacks. Forming a single, continuous channel at a constant or otherwise desired depth from the anterior surface of the cornea is surgically more complicated and necessitates additional steps to ensure that the channel is at a proper depth. Another drawback of continuous ring inserts is that, after insertion, they remain in contact with the initial surgical incision made in the cornea. The ring exerts pressure on the incision, making it more difficult to successfully suture the incision and increasing the possibility of post-surgical infection and reducing the rate of healing. Further, as the flow of nutrients occurs by diffusion from the posterior to the

anterior side of the cornea, post-surgical contact between the insert and the incision site impedes the flow of nutrients to the incision site.

Instead of preformed ring inserts, other prior art techniques for correcting visual aberrations include the use of a settable polymer or polymer gel. For example, U.S. Patent No. 5,095,955 suggests forming an intracorneal ring by introducing a settable polymer or gel into an intrastromal channel which has been previously made, and allowing the polymer to set. This procedure does not allow the surgeon to specify the precise shape of the resulting ring. Moreover, since the shape and length of the gel conforms to that of the intrastromal channel, the gel insert cannot be rotated or moved within channel.

Thus, there is a need for an intrastromal corneal insert which overcomes the limitations of prior art inserts. In view of the particular limitations identified above, there is a need for an intracorneal insert which subtends less than 360°. Furthermore, there is a need for an intrastromal corneal insert that has an arc length and angle less than that of the insertion channel. In addition, it is desirable that such a segment have dimensions (*e.g.*, cone angle, thickness, cross-sectional area, arc length, etc.) which vary or are variable between portions of the segment to allow a surgeon to precisely control the dimensions of the insert in order to achieve the desired corneal correction. It is also desirable to provide an assemblage of such segments having dimensions which vary from segment to segment. Additionally, it is desirable to have a segment and a method of inserting the segment at a desired orientation or angle with respect to the cornea which provides for precise corneal adjustment irrespective of the thickness, width, or arc angle of the segment. Moreover, it is contemplated that the desired segments be used to introduce therapeutic or diagnostic materials into the cornea.

## Summary of the Invention

The present invention is directed to an intrastromal corneal insert for effecting a change in the corneal curvature to treat conditions such as astigmatism, myopia, and hyperopia. The insert is an arcuate or arc-shaped segment. The extent of corneal correction by such a segment, for a given cross-sectional configuration, is a function of one or more predefined parameters, including the arc angle, radius of curvature, cone angle, modulus of elasticity, width and thickness of the segment. Particular visual disorders, such as astigmatism, myopia, hyperopia, and astigmatism in combination with either myopia or hyperopia, are correctable by use of these segments.

An aspect of the invention is to effect a change in the curvature of the cornea by providing one or more segments having a selected arc angle and radius of curvature.

A segment of the present invention may also be provided with a mismatching cone angle selected, independently of the segment's size, to impart an additional correction to the corneal tissue when the segment is positioned at the desired location in the cornea. More specifically, the mismatching cone angle can independently effect a change in the radius of curvature and/or the aspheric shape of the cornea can be effected. Thus, the cone angle is chosen based on the change of curvature desired, the starting curvature of the eye, and based on the thickness, radius of curvature, and modulus of elasticity of the segment for a given cross-sectional configuration. The cone angle may be selected to change the curvature of the eye, and to either maintain or alter its original aspheric shape.

Still another aspect of the invention is to effect a change in the curvature of the cornea by providing segments of varying thickness and widths or alternately, varying the thickness of portions of an individual segment. The segments may be used in isolation, in isolated multiples, in cooperative multiples, as segments in a larger assemblage encircling at least a portion of the cornea, or as assemblages to form constructs of varying thickness.

The arcuate inserts have sufficient structural integrity to approximate the shape of some portion of the intrastromal channel into which a segment is to be placed. The segments may be comprised of one or more polymers having a high and/or low modulus of elasticity. Segments having mismatched cone angles over at least a portion of their lengths are required to have a minimum flexural modulus of elasticity of about 3,500 psi, so that the segment retains its ability to exert a mismatched cone angle effect over time. The inserts may further comprise a hydrophilic or hydrophobic material, or may be a hybrid device comprising layered materials. The insert may have an inner portion or be hollow or adapted to be fillable with a biologic agent, drug or other liquid, emulsified, or time-release eye treatment or diagnostic material, or gel or settable polymer.

When the insert is a hybrid, both the inner and outer portions may comprise variously one or more high or low modulus, physiologically compatible polymers or a composite of a low modulus polymer and a high modulus polymer. The inner portion may comprise a gel or a polymeric material which is polymerized *in situ* after introduction into a hollow center layer.

If hydratable polymers are used, they may be hydrated before or after introduction into the intrastromal passageway created by the surgical device used to introduce these devices into the eye. If the insert is made of a hydratable polymer and the outer layer is hydrated before insertion into the eye, the final size of the insert will be set before insertion. If the hydratable polymers are allowed to hydrate within the corneal space, the device (if appropriate polymers are chosen) will swell within the eye to its final size. If prehydrated, the outer layer often provides a measure of lubricity to the device, allowing it to be inserted with greater ease.

Yet another aspect of the present invention is the use of various methods or techniques for changing the refractive characteristics of an eye. Generally, the techniques involve determining the amount of corrective refraction desired, providing an intrastromal channel which traverses at least a portion of the circumcorneal rotation, and introducing one or more of the above described inventive segmented inserts. Specific indications, such as astigmatism, may be rectified by insertion of one or more of the inserts into a partial intrastromal channel to flatten the steeper portions or to steepen the flatter portions or to simultaneously flatten and steepen portions of the anterior corneal surface without insertion of a complete intracorneal ring.

The above is a brief description of some of the features and advantages of the present invention. Other features, advantages, and embodiments will be apparent to those skilled in the art from the following description, accompanying drawings and appended claims.

## Brief Description of the Drawings

Fig. 1 is a schematic representation of a horizontal section of the eye.

Fig. 2 is a schematic illustration of the anterior portion of the eye showing the various layers of the cornea.

Fig. 3 is a schematic representation of an eye showing the average corneal curvature radius and aspheric shape of the cornea.

Fig. 4 is a schematic representation of a hyperopic eye showing the average corneal curvature radius and the aspheric shape of the cornea.

Figures 5A and 5B show respectively a front view and a cross section of a typical intracorneal insert made according to the invention.

Fig. 6 is a diagrammatic cross-sectional view of a cornea showing an imaginary intracorneal ring positioned therein having a matching cone angle and illustrating geometric relationships of the imaginary ring relative to the cornea.

Figs. 7 and 8 illustrate geometric relationships between a mismatching segment and a cornea in accordance with the present invention.

Fig. 9 illustrates another embodiment of the present invention in which one segment is provided with multiple cone angles.

Fig. 10 is a sectional view taken along line 10-10 in Fig. 9.

Fig. 11 is a sectional view taken along line 11-11 in Fig. 9.

Fig. 12 illustrates a further embodiment of the present invention in which two segments are provided with multiple cone angles.

Fig. 13 is a cross-sectional view of a cornea showing segments of the present invention positioned therein and having matching cone angles.

Fig. 14 is a cross-sectional view of a cornea showing segments of the present invention positioned therein and having mismatching cone angles that according to one embodiment of the invention effects the flattening of the corneal anterior surface for treating myopia.

Fig. 15 is a cross-sectional view of a cornea showing segments of the present invention positioned therein and having mismatching cone angles that according to another embodiment of the invention effects the steepening of the corneal anterior surface for treating hyperopia.

Fig. 16 is a frontal view of segments of the present invention having symmetrical areas of added bulk or cross-section.

Fig. 17 shows a segment of the present invention in which the thickness of the segment is varied.

Fig. 18A-C show respectively a front view, a cross-section, and a top view of an embodiment of a segment made according to the present invention.

Fig. 19A-C show respectively a front view, a cross-section, and a top view of another embodiment of a segment made according to the present invention.

Fig. 20A-C show respectively a front view, a cross-section, and a top view of another embodiment a segment made according to the present invention.

Fig. 21A-C show respectively a front view, a cross-section, and a top view of another embodiment a segment made according to the present invention.

Fig. 22A-C show respectively a front view, a cross-section, and a top view of another embodiment a segment made according to the present invention.

Fig. 23A-C show respectively a front view and two cross sections of a soft, filled intracorneal insert made according to the present invention.

Fig. 24 depicts a front view of an end-to-end assemblage of intracorneal segments having no end junctions between the segments. junctions between the inserts to hold them in a particular spatial relationship.

Fig. 25 shows a front view of an end-to-end assemblage of intracorneal segments having junctions between the inserts to hold them in a particular spatial relationship.

Fig. 26 shows a partial cross-sectional view of an end-to-end assemblage of intracorneal segments which are strung on a filament to form a ring.

Fig. 27A and B show respectively a front view and a cross section of an assemblage of intracorneal inserts made according to the invention which overlap at their ends to form a single monolithic device.

Fig. 28A-E schematically depict steps of a procedure for installing the intracorneal segments of the present invention.

Fig. 29A-E schematically depict steps of another procedure for installing the intracorneal segments of the present invention.

## Detailed Description of the Invention

Prior to explaining the details of the inventive devices and methods, an explanation of the physiology of the eye is provided in conjunction with Figs. 1-2. Referring to Fig. 1, a horizontal section of the eye is shown. Globe 11 of the eye resembles a sphere with an anterior bulged spherical portion representing cornea 12. Globe 11 of the eye consists of three concentric coverings enclosing the various transparent media through which the light must pass before reaching the sensitive retina 18. The outermost covering is a fibrous protective portion the posterior five-sixths of which is white and opaque and called the sclera 13, and sometimes referred to as the white of the eye where visible to the front. The anterior one-sixth of this outer layer is the transparent cornea 12.

A middle covering is mainly vascular and nutritive in function and is comprised of the choroid 14, ciliary body 16 and iris 17. Choroid 14 generally functions to maintain

retina 18. Ciliary body 16 is involved in suspending lens 21 and accommodation of the lens. Iris 17 is the most anterior portion of the middle covering of the eye and is arranged in a frontal plane. It is a thin circular disc corresponding to the diaphragm of a camera, and is perforated near its center by a circular aperture called the pupil 19. The size of the pupil varies to regulate the amount of light which reaches retina 18. It contracts also to accommodation, which serves to sharpen the focus by diminishing spherical aberration. Iris 17 divides the space between cornea 12 and lens 21 into an anterior chamber 22 and a posterior chamber 23. The innermost portion of covering is retina 18, consisting of nerve elements which form the true receptive portion for visual impressions.

Retina 18 is a part of the brain arising as an outgrowth from the fore-brain, with optic nerve 24 serving as a fiber tract connecting the retina part of the brain with the fore-brain. A layer of rods and cones, lying just beneath a pigmented epithelium on the anterior wall of the retina serve as visual cells or photoreceptors which transform physical energy (light) into nerve impulses.

Vitreous body 26 is a transparent gelatinous mass which fills the posterior four-fifths of globe 11. At its sides it supports ciliary body 16 and retina 18. A frontal saucer-shaped depression houses the lens.

Lens 21 of the eye is a transparent bi-convex body of crystalline appearance placed between iris 17 and vitreous body 26. Its axial diameter varies markedly with accommodation. Ciliary zonule 27, consisting of transparent fibers passing between ciliary body 16 and lens 21 serves to hold lens 21 in position and enables the ciliary muscle to act on it.

Referring again to cornea 12, this outermost fibrous transparent coating resembles a watch glass. Its curvature is somewhat greater than the rest of the globe and is ideally spherical in nature. However, often it is more curved in one meridian than another giving rise to astigmatism. The central portion of the cornea is called the optical zone with a slight flattening taking place outwardly thereof as the cornea thickens towards its periphery. Most of the refraction of the eye takes place through the cornea.

Referring to Fig. 2, a more detailed drawing of the anterior portion of the globe shows the various layers of cornea 12 comprising an epithelium 31. Epithelial cells are rich in glycogen, enzymes and acetylcholine and their activity regulates the corneal

corpuscles and controls the transport of water and electrolytes through the lamellae of the stroma 32 of cornea 12.

An anterior limiting lamina 33, referred to as Bowman's membrane or layer, is positioned between the epithelium 31 and stroma 32 of the cornea. Stroma 32 is comprised of lamella having bands of fibrils parallel to each other and crossing the whole of the cornea. While most of the fibrous bands are parallel to the surface, some are oblique, especially anteriorly. A posterior limiting lamina 34 is referred to as Descemet's membrane. It is a strong membrane sharply defined from stroma 32 and resistant to pathological processes of the cornea.

Endothelium 36 is the most posterior layer of the cornea and consists of a single layer of cells. Endothelium cells function to maintain the transparency of cornea 12. Limbus 37 is the transition zone between the conjunctiva 38 and sclera 13 on the one hand and cornea 12 on the other.

Fig. 3 shows the globe of the eye having a cornea 12 with an average spherical radius of curvature 41 and a positive aspheric shape. By "average spherical radius of curvature" we intend the radius of the circle defined by the points at the periphery 45 of the cornea near the limbus of the eye and having a center 46. By "positive aspheric shape" we mean that the distance 47 from that center 46 to the anterior center of the cornea is greater than the average spherical radius of curvature, that is, the anterior surface of the cornea flattens as it progresses from the center 44 to its periphery 45. As shown in Fig. 3, when parallel rays of light pass through the corneal surface, they are refracted by the corneal surfaces to converge eventually near retina 18 of the eye. The diagram of Fig. 3 discounts, for the purposes of this discussion, the refractive effect of the lens or other portions of the eye.

The eye depicted in Fig. 4 is hyperopic because the light rays from the periphery of the cornea refract into focus at a point behind the retinal surface. Further, the eye depicted in Fig. 4 has does not have the same aspheric shape as that shown in Fig. 3. Distance 47 from center 46 to the anterior surface of the cornea is about the same as or less than the average spherical radius of curvature 41 and the cornea does not flatten from center 44 to periphery 45 but rather plateaus or even dips at its center. If an intracorneal segment with a flat mismatched cone angle, according to the present invention and as will be described in detail below, is implanted into the cornea shown in Fig. 4, the light rays refracted by the

now steepened corneal surface will be refracted at a larger angle and thus converge at a more near point such as directly on the retina. Further, selection of an intracorneal segment having a mismatched cone angle may allow for the eye to obtain a more positive aspheric shape similar to that shown in the Fig. 3 eye.

With the background discussion of Figs. 1-4 in hand, it should be understood that the device and method of the present invention is for the adjustment of at least a portion of an annular chord of the cornea to improve the vision of the eye. According to the present invention, one or more arcuate polymeric segments having predefined arc angles, radius of curvature, matching or mismatching cone angles, thicknesses and/or widths, and modulus of elasticity, or combinations thereof for changing the refractive properties of an eye. Each of the inventive aspects of the segments is discussed in detail below.

For purposes of discussing the arc length or arc angle of the segments of the present invention, and how variations in these parameter effect the shape of a cornea, Figure 5A shows a front view of a typical insert made according to the invention and Figure 5B shows a cross section of that insert. As is shown in Figure 5A, the arcuate segment 100 is a portion of the circle and subtends some specific amount of a circumference of the cornea (at some chosen radius) equal to a value of "α" or "arc angle." The particular arc angle value is selected based upon the indication to be corrected and upon the particular configuration of the segment (or segments) used. The arc angle is related to the arc length ($L_\alpha$), the ratio of arc length to arc angle being defined by the expression

$L_\alpha \quad 2\pi R_{cc} \times (\alpha/360°)$, for a given radius "r" of a segment.

For definitional purposes, the opposite ends of a single segment do not meet and subtend less than 360° when the segment is inserted into an intrastromal channel. However, if two or more segments are joined or used in conjunction with each other, the sum of the values of "α" may be any of a wide range of values up to and including 360°. It should be noted that when a group of segments is used having a sum of arc angles equal to or greater than 360° , the advantage of not having the segment in contact with the corneal entry incision is lost.

Another important parameter of the segments of the present invention is the radius of curvature ($R_{cc}$,). The radius or radius of curvature of a segment is related to the rate of change of its curve relative to a fixed axis, or in other words, is related to the radius of the ring that can be configured from that particular segment. Selection of the radius of

curvature for a particular segment is dependent upon the segment's design and shape, the correction to be effected, and the radius of the channel formed in the cornea. For the majority of vision problems to be treated, the radius of curvature of a segment of the present invention which is inserted circumferentially about the cornea is between about 1.5 mm and 4.25 mm.

Referring now to Fig. 5B, there is shown a radial transverse section of segment 100 having a hexagonal cross-sectional shape, one of a variety of suitable cross-sectional shapes for the segments of the present invention. The thickness of the segment, designated with reference character "t", is generally between about 0.05 mm to 0.48 mm, and preferably between about 0.15 and 0.45.

Although a particular segment configuration has been described above, segments of other cross-sectional shapes, including but not limited to ovaloid and rectangular shapes, also may be used provided their respective maximum radial transverse cross-sectional dimensions are within the allowable ranges defined above. Illustrative examples of other suitable shapes are discussed in more detail below.

Returning to Fig. 5B, for purposes of describing the cone angle(s) of the segments of the present invention, reference is made to an imaginary or phantom ring 102 having cross-sectional shape and thickness dimensions identical to those of the segment to be inserted, and having a diameter configured from the segment having phantom ends which extend to meet each other. The radial transverse cross-section of the segment is the cross-section that would cut through the diameter of such an imaginary ring 102 superimposed on the insertion site. As shown in Fig. 5B, the components of the radial transverse cross-section of imaginary ring 200 are the cross-sectional area of segment 100 and phantom portion 104 (shown in phantom).

The cone angle θ of imaginary ring 102, and thus segment 100, is defined, for example, as the angle between the plane of the flat surface 50 that imaginary ring 102 rests on and a line drawn between points 52 of the cross-section that rests on the flat surface and point 54 on the cross-section that is farthest from the point where imaginary ring 102 rests on the flat surface. In other words, cone angle θ the angle formed between the major axis of a radial, transverse cross-section (*e.g.*, axis 56 as shown in Fig. 5B) and surface 50. Alternatively, cone angle θ can be defined with reference to the angle formed by the intersection of major axes 56, angle ϕ, where $\theta = (180-\phi)/2$.

Referring to Fig. 6, an imaginary ring, such as imaginary ring 102 configured from segment 100 described above, is shown inserted into cornea 12. Imaginary ring 102 is shown having a cone angle matched to the corneal architecture prior to insertion. A matching cone angle of a segment can be described with respect to the cone angle of imaginary ring 102. A matched cone angle of imaginary ring 102 may generally be considered to be one that matches the angle defined by a particular line 62 that is tangent to the anterior surface of the cornea 12. That tangent line 62 is obtained by radially projecting the line 66 that extends along the major axis 56' of a radial, transverse cross-section of imaginary ring 102 (*e.g.*, along the line indicating dimension "w" in Fig. 5B) to the anterior corneal surface of the cornea. The major axis 56' of substantially any transverse cross-section of imaginary ring 102 would be parallel to a line in the same plane as that major axis and tangent to the anterior surface of the cornea 12 where the line 64 that bisects the major axis line 66, and is perpendicular thereto, intersects the anterior surface of the cornea. The major axis line 66 is defined as the line which (1) extends along the major axis 56' and (2) is bounded by the outer surface of the segment. A matching cone angle may vary according to changes in corneal shape and to the radial dimension of the segment used.

Conversely, a mismatching cone angle of imaginary ring 102 is one in which the major axes 56' of substantially any radial, transverse cross-section of imaginary ring 102 would not be parallel to tangent line 66 at the point where bisecting line 64 is perpendicular to major axis line 66 and intersects the anterior surface of cornea 12.

Referring now to Figs 7 and 8, the concept of a mismatching cone angle of a segment will be described in detail with reference to imaginary ovaloid intracorneal rings (102', 102") superimposed at the insertion site prior to insertion of the cornea. These imaginary rings have dimensions equal to those of the respective segments to be inserted. As shown in the drawings, the major axis (axes 150 and 152 in Figs. 7 and 8, respectively) of substantially any radial, transverse cross-section of the ring (segment) are not parallel to a line (lines 160 and 162 in Figs. 7 and 8, respectively), which is in the same plane as the major axis and is tangent to the anterior surface of the cornea at the point where the line (line 170 and 172 in Figs. 7 and 8, respectfully) that bisects the major axis line (defined as the line extending along the major axis and bounded by the outer surface of the ring (segment)) and is perpendicular thereto, intersects the anterior surface of the cornea.

Alternatively, matching cone angles, and thus mismatching cone angles, can be described relative to an equation. In deriving such an equation to calculate matching cone angles, applicants considered the variables listed below to be important in determining the corneal radius change, $\Delta R_{0s}$, achieved by implanting the ring in the cornea.

$\Delta R_{0s} = f(R_i, \theta, t, d, D_i, R_{cc}, E_y)$ where

$R_i$ = initial corneal radius of curvature (measured along the anterior corneal surface) (see, *e.g.*, Fig. 6B)

$\theta$ = cone angle of the segment

t = segment thickness

d = depth of the segment in the cornea measured radially from the anterior corneal surface to the midpoint of a radial line, extending across the thickest or largest radial dimension (*e.g.*, "t" in Fig. 5B) of the radial, transverse section referenced above with respect to $D_{cc}$ (defined below) and shown, for example, in Fig. 6 where the depth is indicated with reference character "r".

$D_i$ = limbus diameter

$R_{cc}$ = radius of curvature of the segment, where $R_{cc} = D_{cc}/2$ or one half of the diameter of an imaginary intracorneal ring configured from the segment to be inserted (measured center to center, where each center is at the midpoint of the major axis line of a radial, transverse section of the imaginary intracorneal ring. Such centers are shown in Fig. 6, for example, where they are indicated with reference character "c").

$E_y$ = Young's modulus for the segment

$0_s$ = segment cross-sectional area shape factor, which is a function of the ration of LXA to CXA, or

$$= f\ \frac{LXA}{CXA}$$

where LXA is the long axis of the radial, transverse cross-sectional area of the segment and CXA is the circumference of the radial, transverse cross-sectional area of the segment.

These variables are believed to be the dominant ones that will indicate how the segment will perform in changing corneal curvature or shape.

In general, with a high Young's modulus, an increase in cone angle provides an increase in the minus correction which means an increase in the flattening of the cornea. By lowering the cone angle, one induces a positive correction which results in steepening the cornea. Matching the cone angle is dependent on the starting radial curvature of the cornea. $\Delta R_t$ is the expected radius of corneal curvature change induced by segment thickness independent of cone angle for a given transverse, cross-sectional shape of any particular design where the change is measured as the initial radius of corneal curvature (*i.e.*, the radius of curvature of the cornea prior to segment implantation) minus the final radius of corneal curvature (*i.e.*, the radius of curvature of the cornea after segment implantation).

Further examples indicating that increasing the cone angle increases refractive corrections are provided with respect to data obtained from tests conducted on human eye bank eyes. Cone angles of 31° and 43° provided refractive corrections of about ---2.8 and -4.4 diopters, respectively. Although the segment cone angles varied, each segment had a thickness (t) of about 0.15 mm and was inserted at a depth (d) in the cornea of about 0.42 mm.

Based on the variables listed above, the following equation, which defines a matching cone angle for a given $D_{cc}$ (which is equal to 2 $R_{cc}$) $_{Ri}$ and d, was derived.

(1) $$\theta = \sin^{-1} \frac{D_{cc}}{2(R_i-d)}$$, where

$\theta$, $D_{cc}$, $R_i$ and d are as defined above.

The following table provides matching cone angle values ($\theta$) in degrees rounded to the nearest tenth of a degree for a segment implanted at a depth of 0.42 mm and for an initial corneal radius of curvature ($R_i$) ranging from 7.6-7.9 mm (which is the typical range in the population) and center to center diameters ($D_{cc}$) ranging from 5.0-8.0 mm according to the above equation.

| | $D_{cc}$ | | | | | | |
|---|---|---|---|---|---|---|---|
| $R_i$ | 5.0 | 5.5 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 |
| 7.6 | 20.2 | 22.5 | 24.7 | 26.4 | 24.1 | 31.5 | 33.7 |
| 7.7 | 20.1 | 22.2 | 24.3 | 26.5 | 28.7 | 31.0 | 33.3 |
| 7.8 | 19.8 | 21.9 | 24.0 | 26.1 | 28.3 | 30.5 | 32.8 |
| 7.9 | 19.5 | 21.6 | 23.6 | 25.8 | 27.9 | 30.1 | 32.3 |

The above calculations are merely exemplary and not intended to limit the invention. For example, the implantation depth "d" may range from about 0.10-0.50 mm, even though a value of 0.42 mm is used throughout the above calculations for purposes of example.

A mismatching cone angle is one that does not equal the cone angle described in equation (1) for a given $D_{cc}$ (equal to $2R_{cc}$), $R_i$ and d. Thus, for example, given a $D_{cc}$ of 7.0 mm, an $R_i$ of 7.6 mm and a "d" of 0.42 mm, a mismatching cone angle would be any cone angle that is not equal to 24.1 degrees.

Another equation for describing a cone angle that is a matching cone angle is preferred when accounting for segment thicknesses above about 0.15 mm, which provides sufficient thickness to flatten the cornea independent of cone angle. According to this refined equation:

$$(2) \qquad \theta = \sin^{-1} \frac{D_{cc}}{2[(R_i - d) + |\Delta R_t|]}, \quad \text{where}$$

$\Delta R_t$ = the expected radius of corneal curvature change induced by segment thickness independent of cone angle for a given transverse, cross-sectional shape of any particular segment design. Alternatively, $\Delta R_t$ can be described as the initial radius of corneal curvature minus the final radius of corneal curvature as previously described above where $\Delta R_t$ is determined based only on the change induced by the segment thickness independent of cone angle for a given radial, transverse cross-sectional shape of any segment.

Thus, when accounting for such thicknesses, a mismatching cone angle is one that does not equal the cone angle described in equation (2) for a given $D_{cc}$ (equal to $2R_{cc}$), Ri, d and ΔRt.

The discussion of cone angle of segments has, thus far, been limited to segments having a constant cone angle across its length. However, segments having a cone angle which varies along the length of the segment or, in other words, a segment having multiple cone angles is also contemplated by the present invention. Referring now to Figs. 9-11, a segment having more than one cone angle is shown. In this embodiment, segment 102''' is provided with multiple cone angles. This construction is particularly advantageous for treating astigmatism (or astigmatism concurrent with either myopia or hyperopia) where the corneal curvature varies in different meridians. In the embodiment shown in Fig. 9, the segment cone angle changes along the circumferential direction thereof. Generally speaking, the segment has a first circumferential region having a first cone angle and at least one other region having a cone angle that differs from said first cone angle.

In the example illustrated in Fig. 9, the segment has three circumferential regions with distinct cone angles. Circumferential region 202 has a first cone angle $\theta_1$ as shown in Fig. 10. Circumferential region 202 is followed in the clockwise direction by a second circumferential region 204 having a second cone angle $\theta_2$, as shown in Fig. 11 that substantially differs from the first cone angle $\theta_1$. That is, the cone angle varies enough for treating astigmatism (or astigmatism concurrent with either myopia or hyperopia) as discussed below. Circumferential region 206 follows region 204 with a cone angle similar to that of region 202 in the clockwise direction.

Fig. 12 shows another embodiment of the present invention. Two segments 210 and 220 are shown positioned opposite each other such that they form a ring-shaped structure having two splits. In the example of Fig. 12, segments 210 and 220 have multiple cone angle values and arc angle and length values which are substantially similar to each other and to segment 102''' of Fig. 9. The cone angles of the respective segments 210 and 220, and of the resulting ring-shaped structure, changes along the circumferential direction thereof. In the example illustrated in Fig. 12, the structure has six circumferential regions with distinct cone angles. Segment 210 has a first circumferential region 212 which has a first cone angle $\theta_1$ as shown in Fig. 10. Circumferential region 212 is followed in the clockwise direction by a second circumferential region 214 having a

second cone angle $\theta_2$, as shown in Fig. 11, that substantially differs from the first cone angle $\theta_1$. Circumferential region 216 of segment 210 follows region 214 with a cone angle similar to that of region 212. Circumferential region 222 of segment 220, which follows region 216 in the clockwise direction, has a cone angle similar to region 216. The cone angle varies again in region 224, which has a cone angle similar to that of region 214 of segment 210. Finally, region 226 of segment 220 has a cone angle similar to that of regions 212, 216, and 222.

As discussed with respect to Figs. 9-11, the optimum values of the respective arc angles and cone angles for a particular segment with a particular cross-sectional area shape is dependent upon the vision problem being treated, the radius of curvature of the segment, and the flexural modulus of the segment. Typically, for treating astigmatism with either myopic or hyperopic problems, two or more segments may be used. The two or more segments may have identical cone angles, thickness, and arc length, but may also differ from each other with respect to one or more of these parameters. Thus, although an intracorneal insert having a particular number of segments each having particular multiple cone angle and arc angle configurations has been shown, other configurations can be used. For example, any number of segments may be used, each having various matching or mismatching cone angle configuration and arc angles for treating an individual's particular problem.

As discussed above, an important aspect of the present invention is that the shape of the anterior corneal surface, and particularly the radius of curvature, may be adjusted by using segments having mismatched cone angles. This aspect is generally illustrated in Figs. 13, 14, and 15 where the effect of matching (Fig. 13) and mismatching (Figs. 14 and 15) cone angles is compared. Each of these three Figures shows a cross-sectional view of a pair of opposing segments similar to those described with respect to Fig. 12.

Fig. 13 shows a pair of opposing segments 300 and 302 having cone angles which match the inner lamaellar architecture. In Figs. 14 and 15, there are shown segment pairs having mismatched cone angles. In other words, their respective cone angles do not match the inner lamaellar architecture. The phantom lines shown in these figures correspond to the outer lines of the cornea section of Fig. 13 and thus provide a reference for the corneal configuration changes caused by the respective segment pairs with mismatching cone angles. Referring particularly to Fig. 14, segments 304 and 306 are shown with cone

angles greater than those shown in Fig. 6. The larger cone angle twists adjacent portions of the cornea outward and flattens the central region of the cornea between segments 304 and 306 as shown in the drawing. This particular configuration is helpful in treating myopia. In contrast, Fig. 15 shows a pair of segments 308 and 310 having cone angles less than that shown in Fig. 13. This smaller cone angle effects a steepening of the corneal surface as shown in the drawing and is helpful in treating hyperopia.

Thus far in this description of the present invention, one or more segments having one or more mismatched cone angles have been discussed which are used to effect a change in the radius of curvature of the cornea. Another aspect of the invention is to employ segments, with or without mismatched and/or multiple cone angles, which have varying cross-sections, or otherwise vary in thickness and width along their arcs, to effect the desired alteration of the radius of curvature, and in particular to correct for astigmatism.

Referring now to Figs. 16-17, an embodiment of the segments of the present invention are shown in which the individual segments have at least one region in which the cross-section is thicker or the bulk of that region is more pronounced. Often these segments will have two or more regions at which the bulk is increased. By proper alignment of the various regions of the segment with the areas of the eye that need correction, the proper radius of curvature may be achieved.

In Fig. 16, there is shown two segments 350 and 352 each having a region 354 of added bulk or dimension shown to extend over a region of about 90° of the respective segments. Although regions are shown to be substantially symmetrical, other embodiments in which more than one segment is used and in which the respective regions of enhanced dimension are in an asymmetric configuration are also contemplated by the present invention. The regions of added dimension are critically tailored to correct the astigmatism or astigmatism in combination with either myopia or hyperopia found in a particular eye.

Fig. 17 illustrates a segment 380 in which the thickness of at least one portion of the segment is thicker 382 than another thinner portion 384 of the segment 380. The number of thicker portions of the segment may be one or more depending upon the astigmatic aberration to be corrected.

In general, the thickness of the regions of added bulk may range from about 0.1 mm to less than 0.5 mm. This thickness range is suitable for segments, to treat

astigmatism alone or in conjunction with either myopia or hyperopia, which have arc angle ranges and corresponding constant and variable cone angle ranges discussed above.

Furthermore, the regions 354 subtend an arc of at least about 2° measured from the center of an imaginary ring having identical cross-sectional dimensions and radius of curvature as the segment. More typically the regions of larger dimension will subtend about 10° to 90° and more preferably about 10° to 60°. When multiple sections of added dimension are used, each section may be of the sizes listed above for the single arcs. The sum of all of the subtended arcs for the segment is preferably less than about 350°.

Also contemplated by the present invention is the use of hydratable and swellable polymers for making these segments such that the dimensions, and particularly the thicknesses, of these segments can be adjusted *in situ* after insertion into the cornea. Such aspects of the present invention are discussed in detailed below.

Particular values of the segment parameters discussed above are selected based upon the corneal curvature correction to be effected. The values of some of the individual parameters may be dependent upon the other parameter values selected, such as the radius of curvature and Young's modulus of elasticity of the segment. Accordingly, suitable values for each parameter are generally defined within a range. The following discussion of acceptable value ranges for cone angle, thickness and arc angle is based upon segments having a radius of curvature of about 3.25 mm and comprised of polymeric material having a flexural modulus of elasticity greater than about 3.5 kpsi.

Generally, values for a segment's cone angle, whether constant or variable across the segments length, are between about 0° and 160°, preferably between about 0° and 80°, and more preferably between about 0° and 60°. In general, the value of a segment's arc angle is less than 360°, typically less than 340, more typically 320°, and most typically less than 270°. Segment thickness, whether constant or varying across the length of the segment, ranges from about 0.1 mm to about 0.5 mm.

Many combinations of particular values within the above ranges are acceptable for correction vision problems. However, for purposes of correcting astigmatism where no myopic or hyperopic correction is needed, the combination of variables requires a more specific range of values. Specifically, with segments having a constant cross-sectional area and a constant cone angle along their lengths, suitable arc angles are between about 10° and 90°, preferably between about 20° and 60°, and more preferably between about 30°

and 50°. However, for treatment of pure astigmatism with segments having variable thickness and/or variable or multiple cone angles along their lengths, suitable arc angles are between about 90° and 175°, preferably between about 100° and 175°, and more preferably between about 140° and 165°. Similarly, for treatment of conditions other than pure astigmatism (such as myopia, hyperopia, or combinations of myopia with astigmatism, or combinations of hyperopia with astigmatism) suitable arc angles are between about 90° and 175°, preferably between about 100° and 175°, and more preferably between about 140° and 165°, regardless of whether the segment has a varying or constant thickness or a varying or constant cone angle. It should be noted, that for treating astigmatism in combination with either myopia or hyperopia, a segment having certain other prescribed parameters (such as variable thickness or multiple cone angles) in addition to the above prescribed arc angles may also be used.

The materials used in the segments of the present invention preferably have a shape and sufficient strength such that the segment is not easily damaged by the forces put upon it when it is inserted into the eye. A certain minimum flexural modulus of elasticity is necessary for segments having mismatching cone angles in order to maintain the mismatched angle over time. Thus, with segments having a mismatched cone angle, relatively stiff, physiologically acceptable polymers having a high flexural modulus of elasticity are preferable. Materials having a high flexural modulus of elasticity are those having moduli greater than about 3.5 kpsi.

Acceptable physiological polymers having a sufficiently high modulus of elasticity include polymethylmethacrylate (PMMA), TEFLON, polycarbonate, polysulfones, epoxies, or polyolefins such as polyethylene, polypropylene, polybutylene, and their mixtures and interpolymers. Many of these polymers are known in the art to be appropriately used in hard contact lenses.

The polymeric material making up the segment may be a hybrid which includes more than one polymeric layer. The polymeric layers may be comprised of, for example, one high modulus and one low modulus polymer, or two high modulus polymers, or two low modulus polymers. Low modulus polymers have a Young's modulus of elasticity below about 3.5 kpsi. This class of polymers include physiologically compatible elastomers and such crosslinked polymeric gels as polyhydroxyethylmethylacrylate (Poly-HEMA) or polyvinylpyrrolidone (PVP), polyethylene oxide, or polyacrylates,

polyacrylic acid and its derivatives, their copolymers and interpolymers, and the like as well as biologic polymers such as crosslinked dextran, crosslinked heparin, or hyaluronic acid.

As mentioned above, because a certain minimum amount of segment rigidity is necessary to maintain mismatched cone angles over time, care should be taken to ensure that the overall rigidity of hybrid segments comprised of one or more layers of low modulus polymers is sufficient.

The segments of the present invention may also be hydratable. Partially hydrated or fully hydrated hydrophilic polymers are typically slippery and consequently may contribute to the ease with which the insert may be introduced into the interlamaellar tunnel.

Suitable hydrophilic polymers include polydroxyethylmethacylate (pHEMA), N-substituted acrylamides, polyvinylpyrrolidone (PVP), polyacrylamide, polyglycerylmethacrylate, polyethyleneoxide, polyvinyl alcohol, polyacrylic acid, polymethacrylic acid, poly (N, N-dimethyl amino propyl-$N^1$-acrylamide) and their copolymers and their combinations with hydrophilic and hydrophobic comonomers, crosslinks, and other modifiers. Thermoplastic hydrogels include hydropoly-acrylonitrile, polyvinyl alcohol derivatives, hydrophilic polyurethanes, styrene-PVP block copolymers and the like.

The intrastromal corneal segment may be lubricated with suitable ocular lubricants such as hyaluronic acid, methylethyl cellulose, dextran solutions, glycerine solutions, polysaccharides, or oligosaccharides upon its introduction to help with the insertion particularly if one wishes to insert intrastromal segments of hydrophilic polymers without prior hydration. If a hybrid segment having a hydrophilic polymeric covering or a segment comprising a hydrophilic polymer is inserted into the eye without prior hydration, subsequent to the insertion, the intrastromal segment will swell to its final size or thickness within the eye. This swelling often permits the inclusion of larger intrastromal segments than would normally be accommodated within normal sized intrastromal channels.

Low modulus polymers used in this invention are often absorbent, particularly if they are hydratable, and may be infused with a drug or biologic agent which may be slowly released from the device after implantation of the intrastromal segment. For instance, the low modulus polymer may be loaded with a drug such as dexamethasone to reduce acute

inflammatory response to implanting the device. This drug helps to prevent undesirable scarring or vascular ingrowth toward the intrastromal segment. Similarly, heparin, corticosteroids, antimitotics, antifibrotics, antiinflammatories, anti-scar-forming, anti-adhesion, and antiangiogenesis factors (such as nicotine adenine dinucleotide ($NAD^+$)) may be included to reduce or prevent angiogenesis and inflammation. Clearly, there are a variety of other drugs suitable for inclusion in the intrastromal segment. The choice will depend upon the use to which the drugs are put.

Each of Figs. 18A-C, 19A-C, 20A-C, and 21A-C, shows respectively a front view ("A" drawing) and a cross section ("B" drawing) and a side view ("C" drawing) of various narrow point intracorneal inserts made according to the invention. Although these drawings show narrow points on the inventive inserts, such points are not a critical aspect of the invention. The ends of the inserts may be tapered in both width and thickness, in one or the other of those axes, or may be blunt. Other variations of the ends will be discussed below to the extent necessary to understand the invention. These inserts are "pre-formed" or "pre-shaped." By the use of these terms, it is meant that the insert has sufficient structural integrity to approximate the shape of some portion of the intrastromal channel into which it is to be placed.

Figure 18A shows a front view of a pre-shaped intracorneal insert 400 having ends 402. The intracorneal insert tapers both in width and in thickness to narrow points 402. Viewed in cross section in Figure 18B, the generally smooth convex front surface 404 and planar rear surface 406 may be seen. Figure 18C shows a side view of the segment or insert.

Figure 19A shows a front view of an intracorneal insert 500 having ends 502. Again, the intracorneal insert tapers both in width and in thickness to narrow points 502. Viewed in cross section in Figure 18B, the generally hexagonal shape may be seen. The surfaces most adjacent the anterior surface of the eye and the side just opposite are generally the two longer of the sides. Those generally planar front surface 504 and planar rear surface 506 may be seen. Figure 19C shows a side view of the segment or insert.

Figure 20A shows a front view of an intracorneal insert 600 having ends 602. The intracorneal insert tapers both in width and in thickness to narrow points 602. Figure 20B shows the generally round cross section. The cross section may also be oval-shaped with the major axis of the oval either as the width or the thickness or neither. Figure 20C shows

a side view of the segment or insert which, because of the symmetry of the device, is the same as the top view.

Figure 21A shows a front view of a hybrid intracorneal insert 700 having ends 702. Again, the intracorneal insert tapers both in width and in thickness to narrow points 702. Viewed in cross section in Figure 19B, the generally hexagonal shape may be seen. This set of Figures is to show the concept of a multilayered insert made up of polymers of different characteristics. In this example of a multilayered insert, the hybrid intrastromal segment has inner 702 and outer faces 704 of polymers having low moduli of elasticity. Low modulus polymers are those having a Young's modulus of elasticity below about 3.5 kpsi, more preferably between 1 psi and 1 kpsi, and most preferably between 1 psi and 500 psi. They must be physiologically compatible with the eye. This class of polymers includes most polymeric materials used in soft contact lenses.

The inner portion or core 706 as shown in Figure 21B may be a physiologically compatible polymer having a high modulus of elasticity. As discussed above, high Young's modulus of elasticity is considered to be greater in value than about 3.5 kpsi, preferably 5-10 kpsi, and most preferably 8-10 kpsi.

If hydratable polymers are chosen for the outside layers, the extent to which those outer layers swell upon hydration is dependent upon the type of polymer chosen and, when the polymer is hydratable, upon the amount of cross-linking found in the outer layers 702 and 706, and upon the thickness of the layer. Generally speaking, the more highly linked the hydratable polymer, the smaller the amount of volume change upon hydration. Alternatively, a substantially nonswellable polymer system may be formed of a hydrogel physically interpenetrated by another polymer which does not hydrate, *e.g.*, polyHEMA, to limit its degree of swelling and water absorption.

The thickness of the outer layer depends in large function upon the intended use of the intrastromal segment. If the outer layer is used to provide a swellable outer layer which does not add significantly to the size of the intrastromal segment or is used functionally as a lubricant layer, the other layer may be quite thin -- even to the point of a layer of minimum coverage, perhaps as thin as a single molecular layer.

Of course, the inner and outer layers need not be, respectively, low modulus and high modulus polymers but may instead be multiple layers of low modulus polymers

including an outer hydrophilic polymer layer and an inner hydrophobic polymer; a variety of hydrophilic polymers; etc.

Additionally, the inventive device shown in Figs. 21A-C need not have a inner 704 and outer 702 layers over the entire intrastromal segment. For instance, to alleviate astigmatism, an intrastromal segment having a thicker portion and a substantially thinner portion may be desired. An intrastromal segment having an inner core of a high modulus polymer and an outer covering of a swellable polymer might be chosen. The surgeon would remove a portion of the intrastromal segment's exterior coating or face prior to introducing the intrastromal segment into the eye. Further, and as will be discussed below in greater detail, hydrophilic polymers are more easily infused with therapeutic and diagnostic materials than are the high modulus materials. In the variation just noted, the insert may then be used to deliver the infused therapeutic and diagnostic materials in a greatly delimited of treatment or diagnostic area.

Fig. 22A shows a front view of an wide end intracorneal insert 800 having ends 802. In this variation, the insert tapers only in thickness to form a spade-shaped end 802. Viewed in cross section in Fig. 22B, the generic shape may be seen. Fig. 22C shows the same shape but nearer to the end of the device. This set of figures is to show the concept of a single-tapered end.

Fig. 23A is a front quarter view of a variation of the intrastromal segment 900 made of a low modulus polymer system hydratable outer coating 902. Fig. 23C shows the inner cavity 904. This intrastromal segment may be inserted into the intrastromal space created by the dissector as a covering on a tool similar to the dissector which created the intracorneal channel. Once in position the insertion tool is rotated out of the intrastromal segment leaving the shell within the stroma.

Fig. 23C shows the inner cavity 904 which may be filled with a biologic, a drug or other liquid, or biologically active eye treatment material. These devices may be tied or pinched or crimped or otherwise connected at their point of insertion by known techniques.

The shell 906 may be injected with a settable soft polymer core, allowed to expand to a desired thickness, and set. Polymeric gels which do not polymerize *in situ* are preferred. Suitable injectable polymers are well known but include polyHEMA hydrogel, cross-linked collagen, cross-linked hyaluronic acid, siloxane gels, and organic-siloxane gels such as cross-linked methyl vinyl siloxane gels.

Fig. 24 shows a variation of the invention in which an assemblage of the inventive intrastromal segments 950 are formed into a polymeric ring or, at least, into an assemblage which totals no more than 360° of corneal circumference when assembled into the intracorneal space. The two segments 950 depicted in Fig. 24 may be of any of the individual variations shown in the Figures above and need not be connected in any way.

Fig. 25 shows a similar assemblage in which the intracorneal segments 952 are held together using open holes 954 and a clip 956 which may be a simple wire or other suitable joining device. An assemblage such as is seen in Fig. 25 may be advantageously inserted from a single central opening, as will be described below.

Fig. 26 shows a variation, an assemblage of segments, in which the sections 960 are strung together on a filament 962. The segments 960 have an open pathway along their length (see cutaway) which permits such stringing.

Figs. 27A and B show a variation of the inventive intracorneal inserts in which two or more inserts overlap to form an assemblage. The top view shown in Fig. 27A depicts the assemblage as found in the eye. The assemblage need not be formed of segments of the same or similar width or thickness or material of construction nor need the assemblage be limited to the semicircle shown in Fig. 27A. Although a front-to-back assemblage is depicted in Fig. 27B, the junction between the sections (964 and 966) may be of any other design which allows contact between the adjoining sections and remains relatively immobile after the placement in the cornea. For instance, the design shown in Figures 27A and 27B involves the use of a smooth interface. The intrastromal channel normally exerts a force against the assemblage and will maintain the segments in the depicted relational position within the eye.

Although particular embodiments of segment assemblages have been illustrated in the Figures, other assemblages are acceptable. The segments may be of similar or quite different configurations depending upon the indication to be remedied. For example, rather than overlapping or being positioned end-to-end, the segments may be stacked one on top of the other to form a thicker insert. Additionally, the segments may be inserted in separately produced intrastromal channels which may, or may not, be in communication within the cornea. Such individual insertion will be discussed in more detail below.

The present invention includes methods for inserting the above-described inventive segments into the cornea of the eye in which partial arc segments are introduced into

separate sections of the corneal circumference outside of the optical zone of that cornea. In particular Figs. 28A-E depict a method of inserting more than one segment through more than one entry slit within the cornea. Figs. 29A-F, on the other hand, illustrate a method of inserting one or more segments through only one entry slit with the cornea. Specifics of surgical devices which may be used to make the initial corneal slits and intrastromal channels, *e.g.*, dissectors and supporting devices, may be found in PCT Publication No. PCT/US93/03214, PCT Publication No. WO9320763 entitled "Corneal Vacuum Centering Guide and Dissector," and PCT Publication No. WO09403129 entitled "Hybrid Intrastromal Corneal Ring" the entirety of which are incorporated by reference.

Turning now to a discussion of one of the methods, Fig. 28A shows a frontal view of an iris 800 and a pupil 802. As was described above, the cornea is clear and is not visible in these drawings. First, an entry slit 804 is made radially into the cornea. A dissector blade (not shown) is introduced into the entry slit 804 and turned in the direction of the arrow 806 to form a partial intrastromal channel of a desired length. A second entry slit 808 may then be made in the cornea and a second intrastromal channel be made in the direction of the arrow 810, as shown in Fig. 28B. The first and second channels have been shown to be formed by turning the dissector blade in counter-clockwise and clockwise directions, respectively, for purposes of describing the invention. Alternatively, the entry slits may be made at other radial locations around the cornea, with channels formed in respectively opposite directions form those described. Additionally, the channels may be formed in the same direction, for example, where the entry slits are 180° apart.

Fig. 28C shows the introduction of a first inventive segment 812 into the first entry slit 808. Fig. 28D shows first segment 804 in its final resting position and the introduction of a second segment 814 into the second entry slit 808. Finally, Fig. 28E shows both first segment 804 and second segment 814 in their final position within the cornea. As finally positioned, neither segments 804 and 814 are in contact with the two initial incisions so as to facilitate healing of the incisions. This method demonstrates the flexibility of the procedure in that either clockwise or counter-clockwise insertion is appropriate and the intrastromal channel need not be a complete circle about the cornea.

Figs. 29A-F schematically portray a method for the insertion of the segments described above in which partial arc segments are introduced into separate sections of the

corneal circumference outside of the optical zone area of that cornea through a single entry slit.

Fig. 29A shows the making of an initial entry slit 840 radially into the cornea. A dissector blade (not shown) is introduced into the entry slit 840 and turned in a counter-clockwise direction as indicated by arrow 842 to form a partial intrastromal channel of a desired length or angle, typically from about 0° to 350°. In the illustrated method, the channels are shown to have about a 180° arc. As is shown in Fig. 29B, a second intrastromal channel is made by means of rotating a dissector blade (not shown) in the clockwise from about 0° to 350° in a direction, as indicated by arrow 844, from the same initial entry slit 842. Alternatively, the procedure may begin with forming a channel in the clockwise direction, however, for purposes of this discussion, a procedure that begins with forming a channel in the counter-clockwise direction is described. With either procedure, the channels are formed in opposite directions. The two channels may meet to form one 360° channel, overlap each other, or preferably form one channel which is less than 360°.

Fig. 29C shows the introduction of the first segment 846 into the entry slit 842. Fig. 29D shows the first segment 846 in its final resting position. Fig. 29E shows the introduction of the second segment 848 into the entry slit 840. Finally Fig. 29F shows both first segment 846 and second segment 848 in their final position within the cornea. Again, both segments are positioned away from the incision point to facilitate healing of the incision.

Alternatively, the present invention contemplates forming one channel having an arc angle of 350°, for example, into which two or more segments may be introduced and positioned within the channel as desired.

Because of the nature of certain of the segments of the present invention, a large measure of adjustability is available in the process of inserting the segments. For instance, it has been found that when using various inserts (particularly with ocular lubricants) that the inserts may be "pushed" nearly 180° or more around a previously created intrastromal channel for insertion and then easily removed, if so desired. This observation means that the following procedure may be used. The eye of a person having myopia and/or astigmatism may be measured to determine the proper amount of correction needed. From this information, the size and placement of one or more segments may then be chosen. After insertion in the appropriate channels, the vision of the eye might again be measured.

If insufficient correction of an indication is found, the insert may need to be rotated within the channel or be withdrawn (partially or completely) and trimmed prior to complete re-insertion. Alternately, it may be necessary to replace the segment with another segment having a different cone angle, radius of curvature, arc angle, or thickness in order to more accurately treat the particular corneal problem. Such adjustability is not normally available when dealing with prior art inserts such as gel-based rings or with surgical techniques based on radial keratotomy.

The following two examples, based on clinical procedures, are intended to further illustrate the method discussed with respect to Figs. 29A-F but are not intended to limit the invention in any way.

EXAMPLE 1

The eye at issue required correction of myopia. It was determined that the amount of correction required was between -2.0 to -2.5 diopters. Based on the amount of correction to be achieved, it was determined that two segments, each having a thickness of 0.3 mm, an arc angle of 150°, and a constant cone angle of 34°, should be symmetrically positioned about the vertical axis. The insertion procedure involved making an entry slit, similar to that shown in Fig. 29A, and forming a counter-clockwise channel having an arc of 210°. Then, from the same entry slit, a clockwise channel also having an arc of 210° was formed in the opposite direction, similar to that shown in Fig. 29B. The two segment were then inserted into their respective channels and positioned symmetrically opposite each, similar to that shown in Fig. 29F. Measurements showed that the desired power correction of -2.5 diopters was achieved.

EXAMPLE 2

The eye at issue in this example was astigmatic, requiring -3.0 diopters of correction. Here, two segments, each having a thickness of 0.40 mm, a cone angle of 34°, and an arc angles of 45°. The same insertion procedure was used to position the segments symmetrically opposite each other about the vertical axis, similar to the arrangement shown in Fig. 29F. Measurements were taken showing a correction of only -5.0 diopters, -2.0 diopters in excess of the desired correction. The segments were then rotated out of the channels and replaced with segments having the same arc and cone angles but having a thickness of 3.0 mm. Measurements then showed that the increase in thickness of the segments had achieved the desired -3.0 diopter correction.

The above is a detailed description of particular embodiment of the invention. It is recognized that departures from the disclosed embodiments may be made within the scope of the invention and that obvious modifications will occur to a person skilled in the art. The full scope of the invention is set out in the claims that follow their equivalents. Accordingly, the claims and specification should not be construed to unduly narrow the full scope of protection to which the invention is entitled.

Claims:

1. An intrastromal corneal insert comprising a preformed, physiologically compatible, polymeric arcuate segment having an arc angle less than 360° and in which at least one of the following characteristics varies over the arc angle of the segment: cone angle, width, thickness, and modulus of elasticity.

2. The insert of claim 1 wherein the cone angle varies in the range of 0° and 180°.

3. The insert of claim 2 wherein the cone angle varies in the range of 0° and 60°.

4. The insert of claim 1 wherein the cone angle varies continuously.

5. The insert of claim 1 wherein the cone angle varies step wise.

6. The insert of claim 1 wherein the thickness varies in the range of about 0.1 mm and about 0.5 mm.

7. The insert of claim 1 wherein said segment has an arc angle suitable for treating pure astigmatism.

8. An intrastromal corneal insert for implantation in a cornea having an anterior surface, said insert comprising an arc-shaped segment having a radius of curvature, a cone angle, an outer surface, a major axis for each radial, transverse cross-section thereof ,and a major axis line for each said cross-section, each major axis line defined as the line that extends along a respective major axis and is bounded by said outer surface of said arc-shaped segment, said cone angle being one that if an imaginary ring, having the same radius of curvature, major axes, and major axes lines as said arc-shaped segment, were superimposed at an insertion site in said cornea prior to actual insertion of said arc-shaped segment, the major axis of substantially any radial, transverse cross-section of said imaginary ring would not be parallel to a line in the same plane as that major axis and tangent to the anterior

surface of the cornea at the point where a line, that bisects the major axis line and is perpendicular thereto, intersects said anterior surface of the cornea.

9. The arc- shaped segment of claim 8 wherein said cone angle varies along the circumferential direction of said segment.

10. The arc-shaped segment of claim 9 wherein said segment has a first circumferential region having a first cone angle and at least one other region having a cone angle that differs from said first cone angle.

11. The arc-shaped segment of claim 8 having multiple cone angles.

12. The arc-shaped segment of claim 11 wherein said cone angle is selected to maintain said anterior surface in substantially an aspheric shape.

13. A surgical system or kit for use in correcting refractive characteristics of an eye comprising at least two intrastromal corneal inserts that are preformed, physiologically compatible, polymeric arcuate segments having an arc angle less then 360° which differ from each other in at least one of the following characteristics: cone angle, radius of curvature, width, thickness, and modulus of elasticity.

14. The system or kit of claim 13 wherein the inserts differ in cone angle and their cone angles are in the range of 0° and 180°.

15. The system or kit of claim 14 wherein the inserts differ in thickness and their thickness are in the range of about 0.1 and 0.5 mm.

16. The system or kit of any of claims 13-15 wherein the inserts have different arc angles.

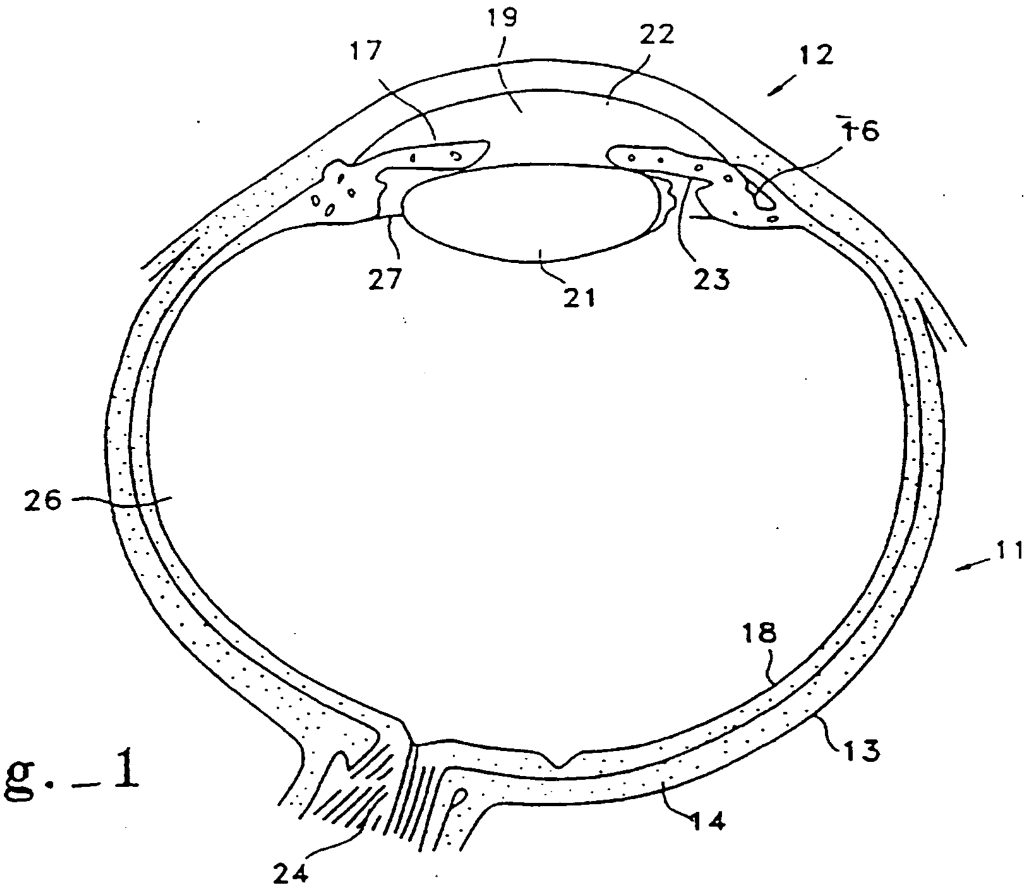



Fig._1

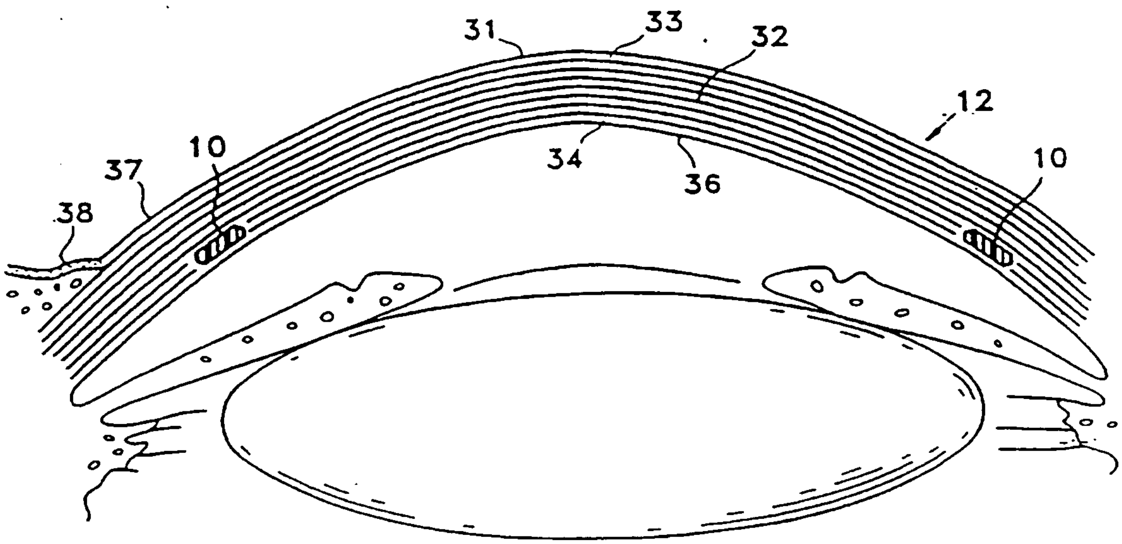
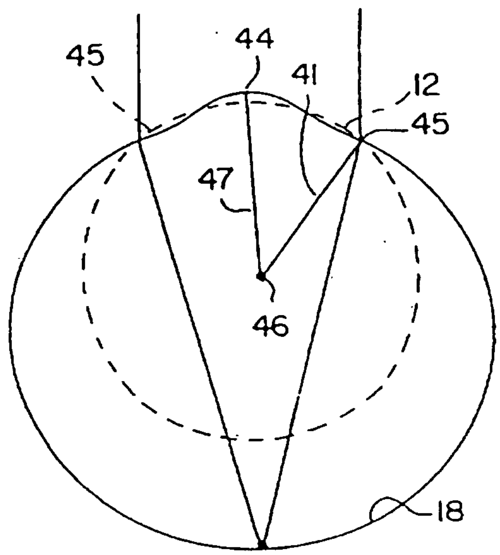
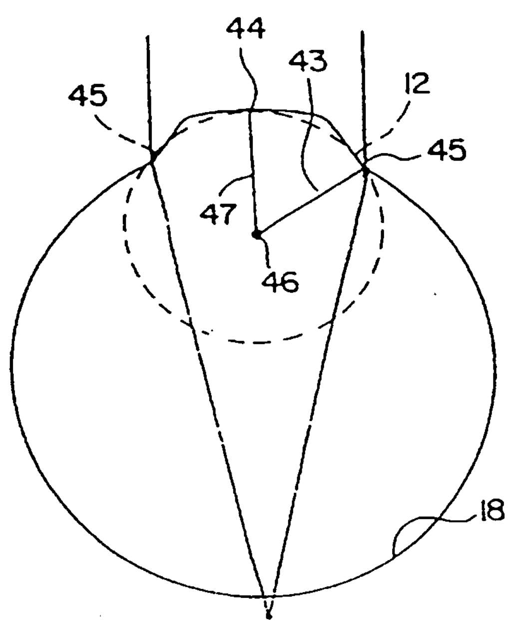



Fig._2




F I G._3




F I G._4

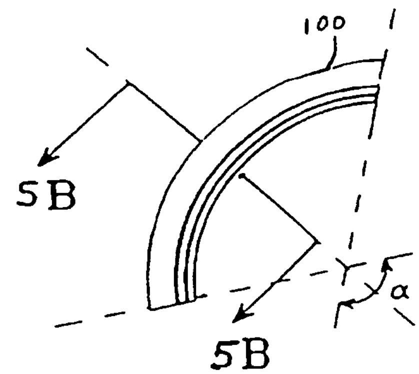



Fig._5A

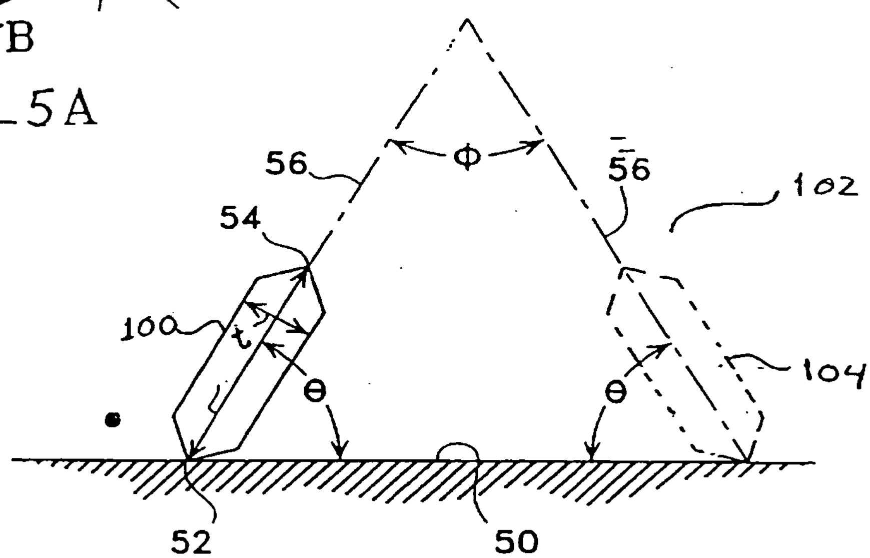



Fig._5B

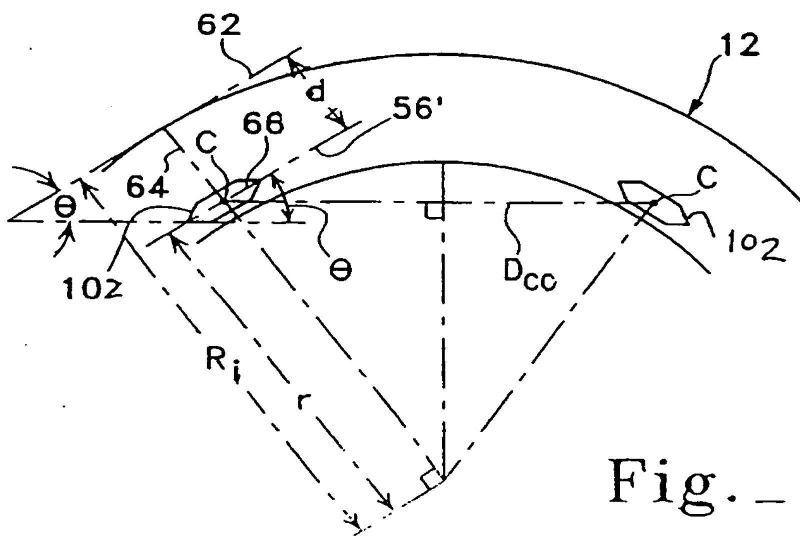



Fig._6

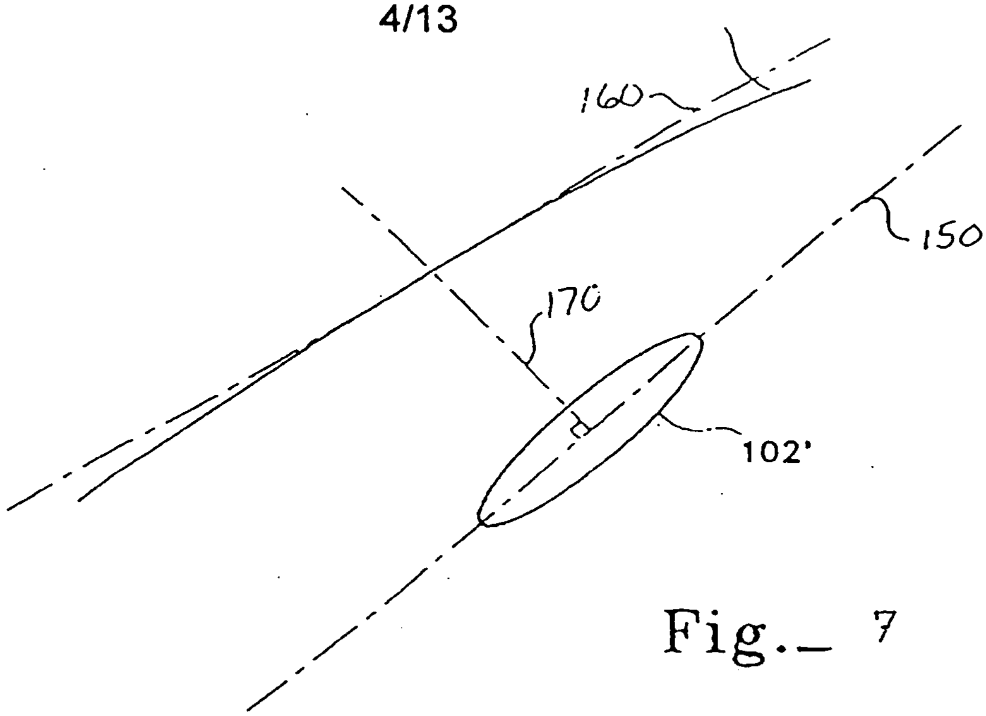



Fig. 7

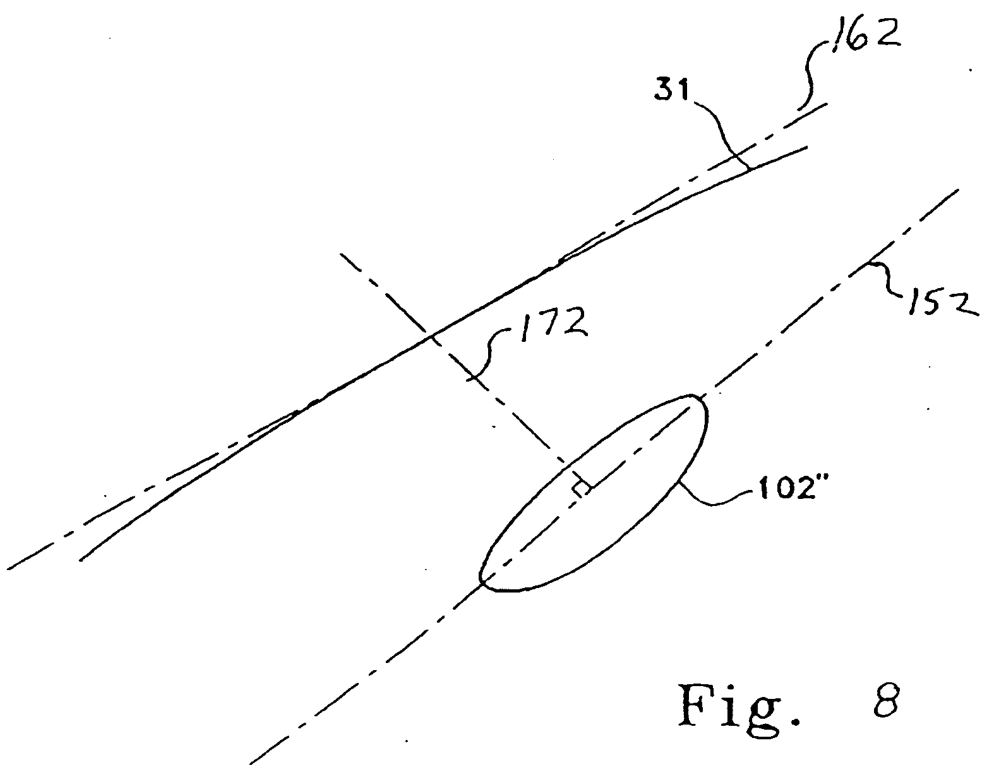



Fig. 8

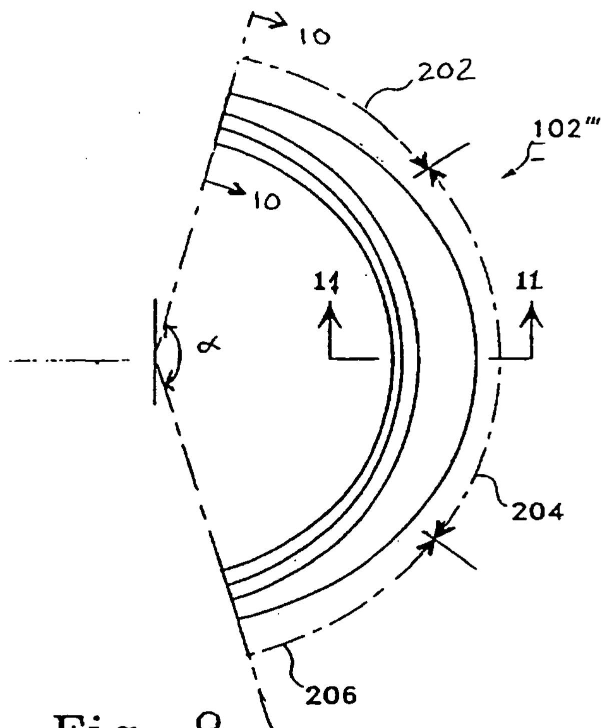



Fig._9

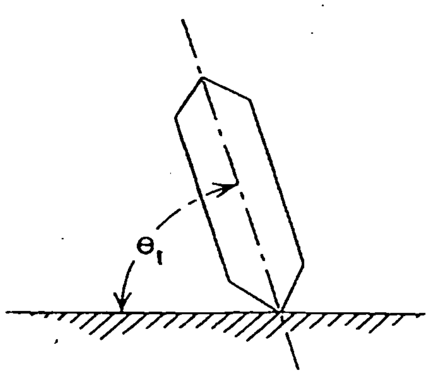



Fig._10

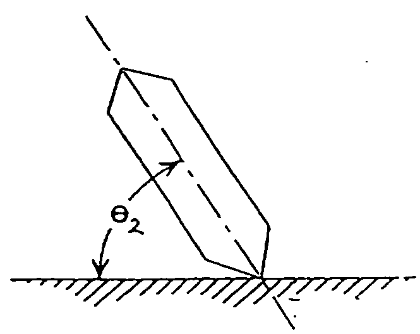



Fig._11

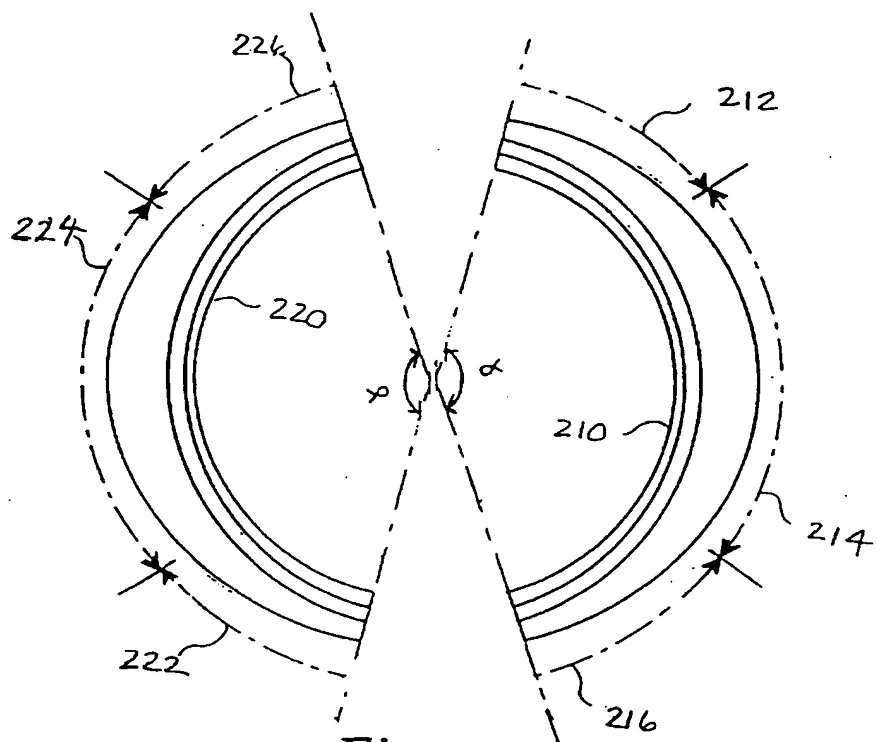



Fig. _12

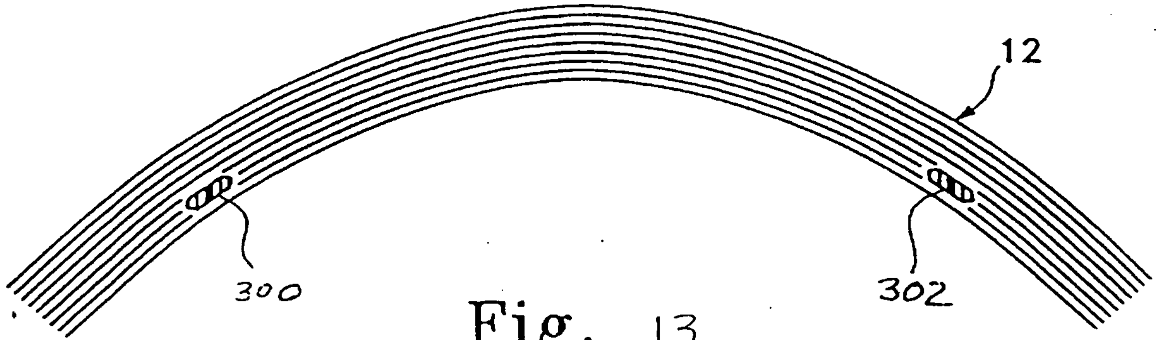



Fig._ 13

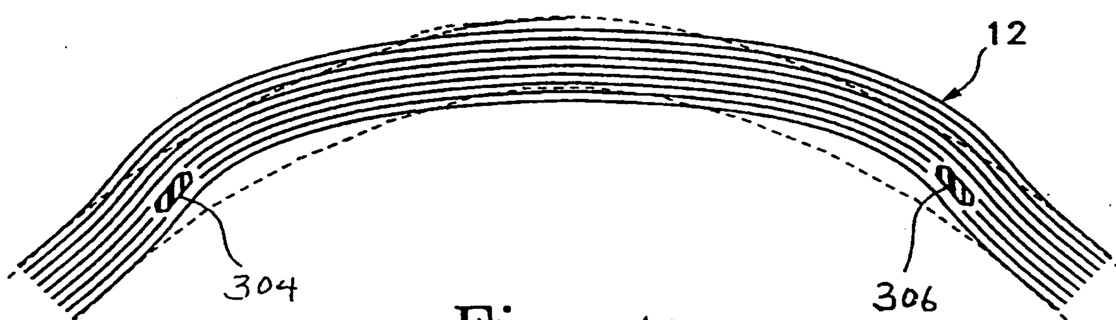



Fig._ 14

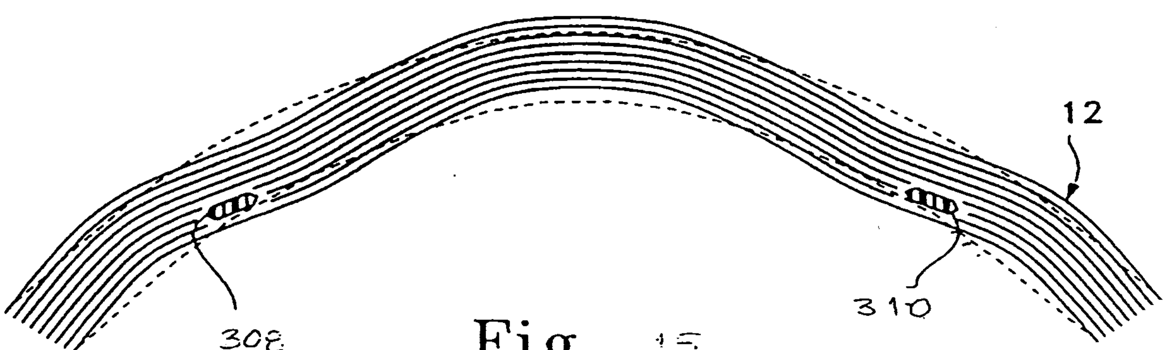



Fig._ 15

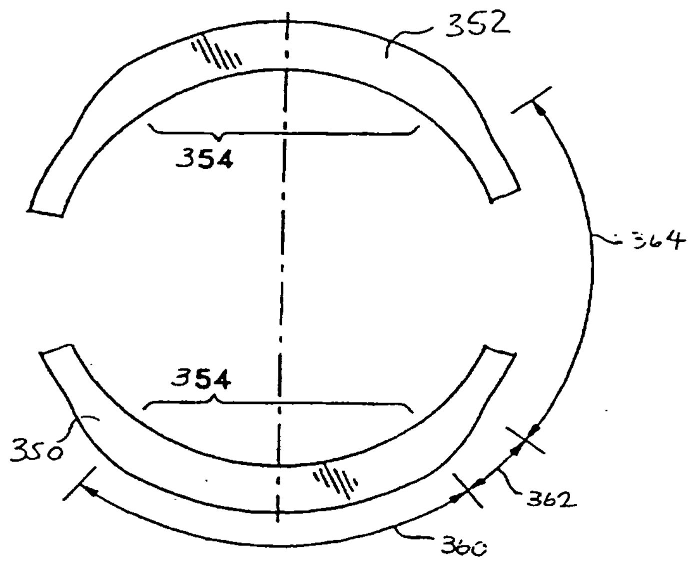



FIG. 16

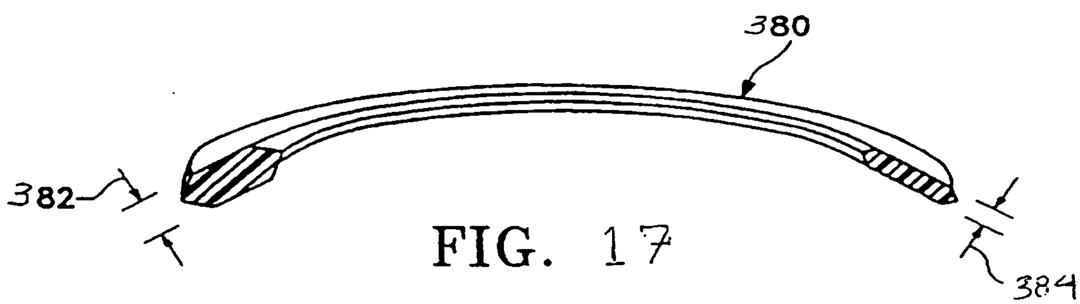



FIG. 17

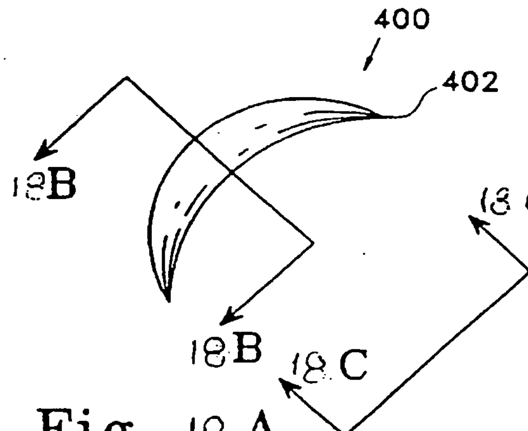



Fig. 18-A

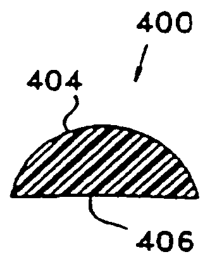



Fig. 18 B

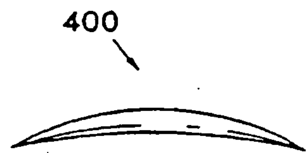



Fig. 18 C

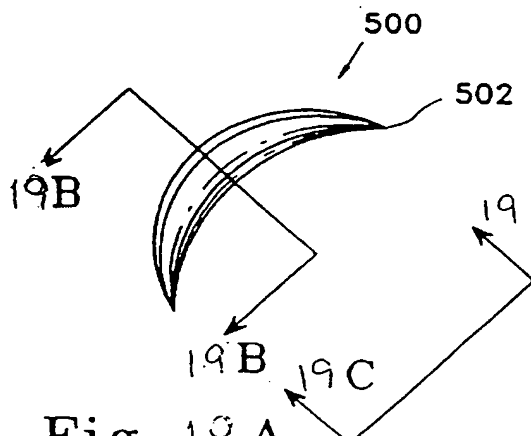



Fig. 19 A

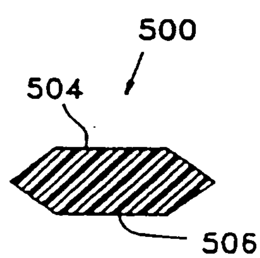



Fig. 19B

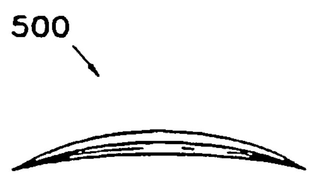



Fig. 19 C

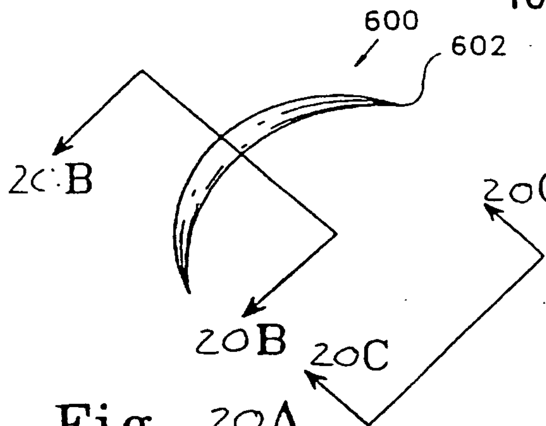



Fig. 20A

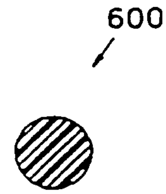



Fig. 20B

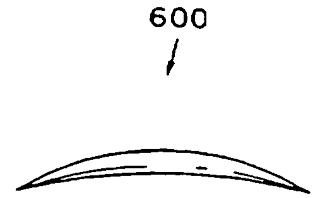



Fig. 20C

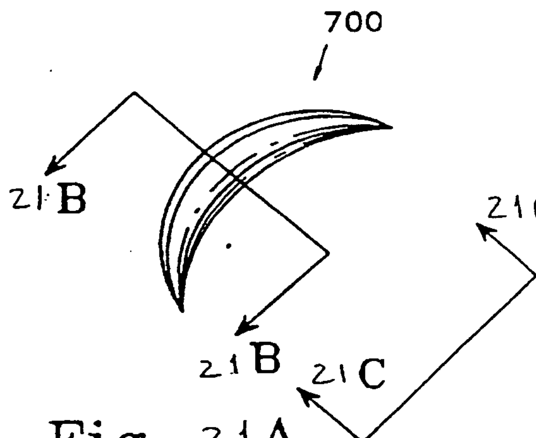



Fig. 21A

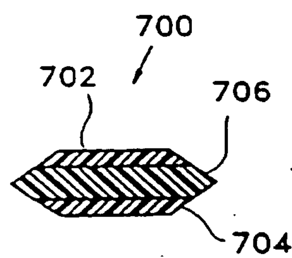



Fig. 21B

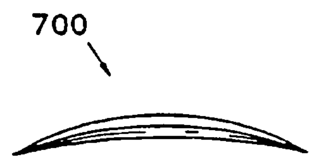



Fig. 21C

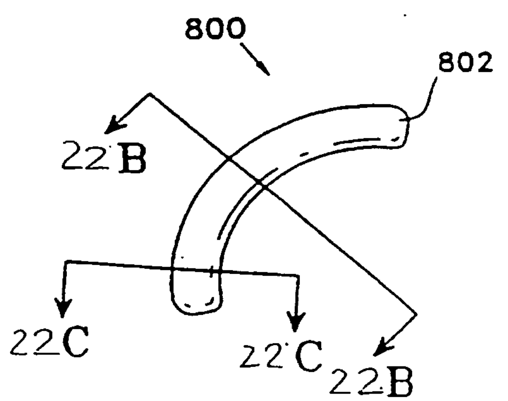



Fig. 22A

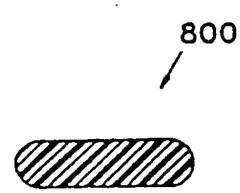



Fig. 22B

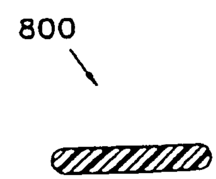



Fig. 22C

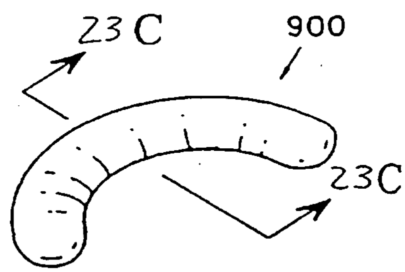



Fig. 23A

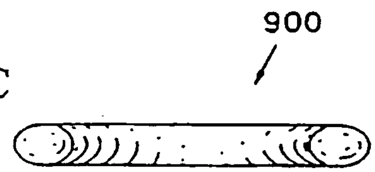



Fig. 23B

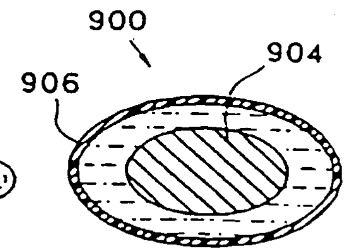



Fig. 23C

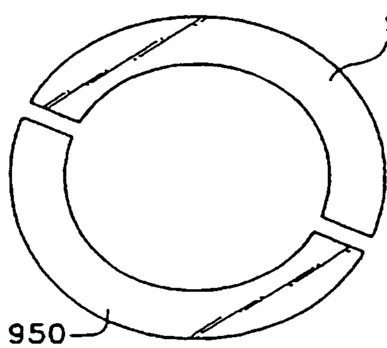



Fig. 24

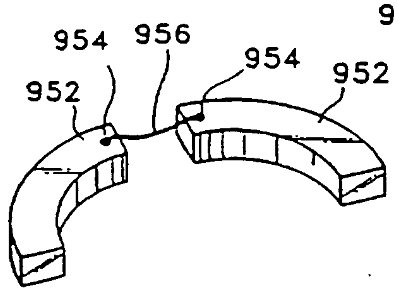



Fig. 25

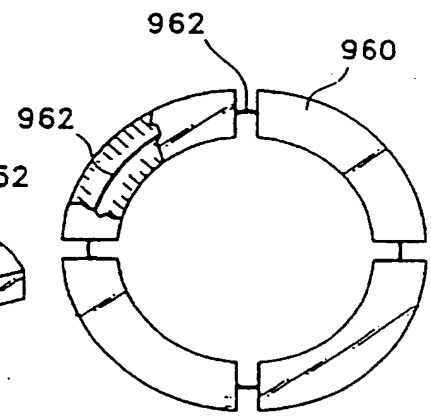



Fig. 26

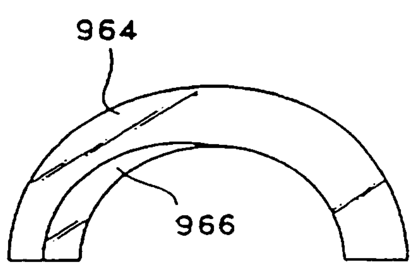



Fig. 27 A

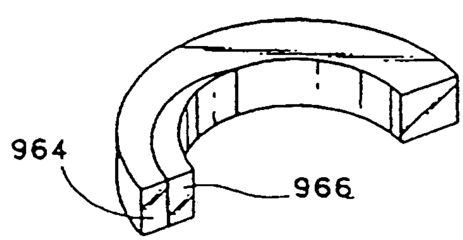



Fig. 27 B

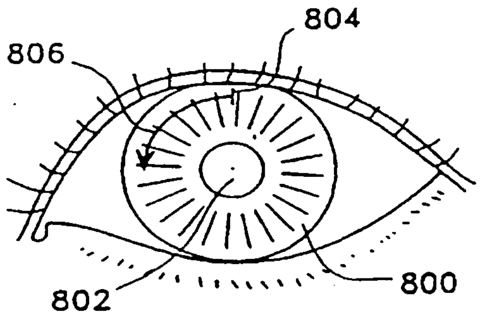



Fig. 28A

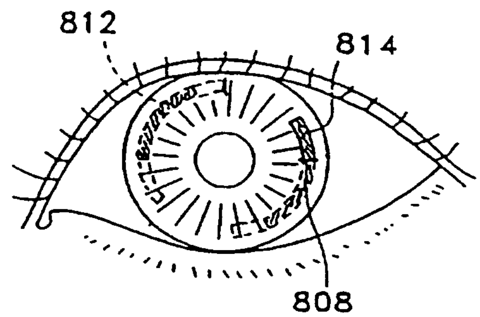



Fig. 28D

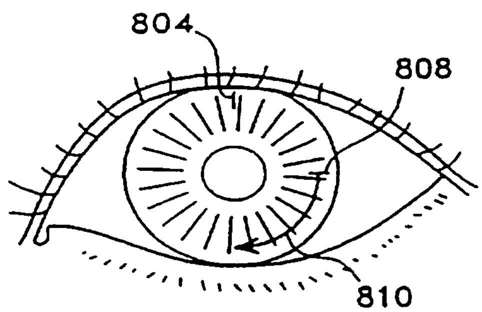



Fig. 28B

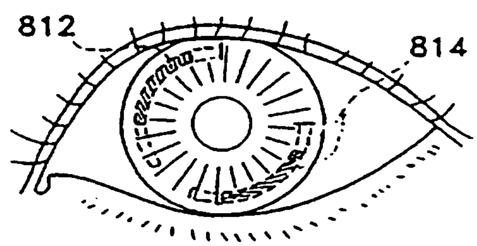



Fig. 28E

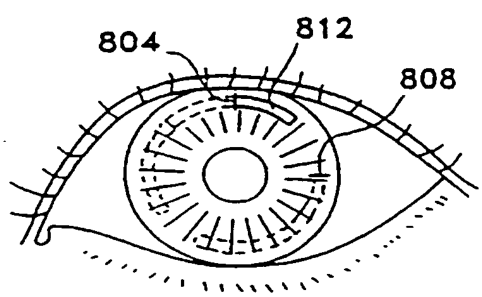



Fig. 28C

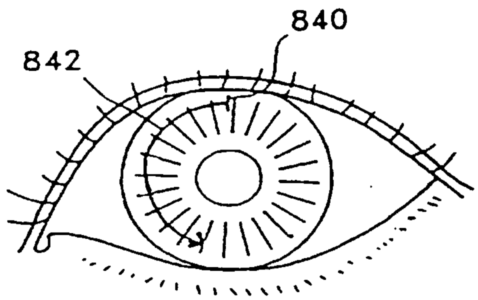



Fig. 29A

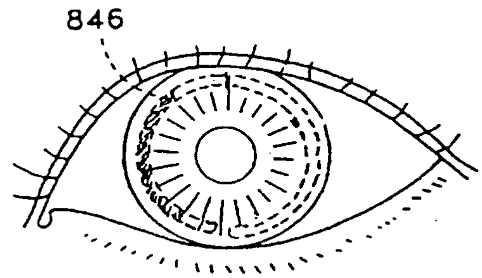



Fig. 29D

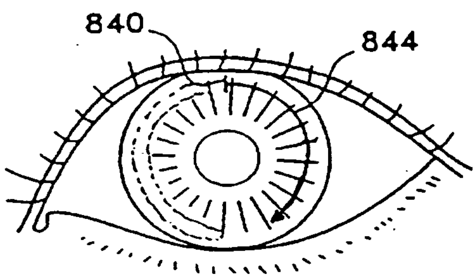



Fig. 29B

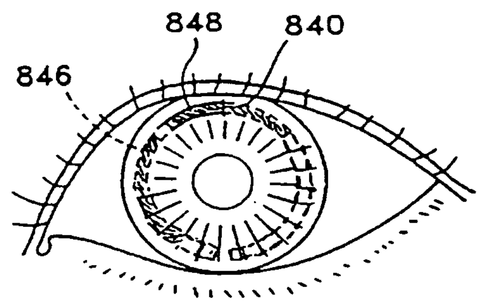



Fig. 29E

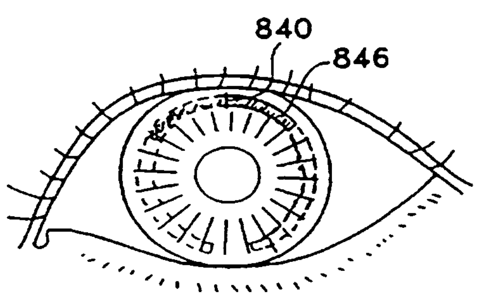



Fig. 29C

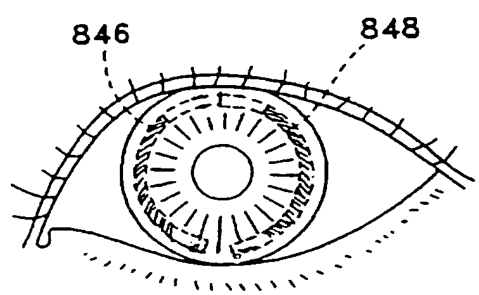



Fig. 29F

# INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 97/01411

**A. CLASSIFICATION OF SUBJECT MATTER**
IPC 6 A61F2/14

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X<br>A | WO 95 15719 A (KERAVISION) 15 June 1995<br>cited in the application<br>see the whole document | 1,6,7<br>8,12,13,15 |
| X | WO 95 05789 A (KERAVISION) 2 March 1995<br>see page 9, line 1 - line 24; figures | 8 |
| X | WO 95 03755 A (KERAVISION) 9 February 1995<br>see page 19, line 19 - line 27; figures | 13 |
| A | WO 95 03747 A (KERAVISION) 9 February 1995 | |
| P,X | WO 96 26690 A (KERAVISION) 6 September 1996<br>see abstract; claims 8,12-15; figures | 8,13 |

[ ] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

1

Date of the actual completion of the international search: 10 June 1997

Date of mailing of the international search report: 18.06.97

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer
Steenbakker, J

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 97/01411

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. Claims: 1-7,13-16 Intrastromal corneal insert or a surgical system with at least one variable characteristic (cone angle width, thickness, and modulus of elasticity).
2. Claims: 8-12 Intrastromal corneal insert having one specific defined cone angle.

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern al Application No
PCT/US 97/01411

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---|---|---|
| WO 9515719 A | 15-06-95 | US 5405384 A | 11-04-95 |
| | | AU 1431795 A | 27-06-95 |
| | | BR 9408262 A | 10-12-96 |
| | | CA 2178478 A | 15-06-95 |
| | | EP 0732891 A | 25-09-96 |
| WO 9505789 A | 02-03-95 | AU 7673494 A | 21-03-95 |
| | | BR 9407359 A | 29-10-96 |
| | | EP 0746272 A | 11-12-96 |
| WO 9503755 A | 09-02-95 | AU 7515694 A | 28-02-95 |
| | | BR 9407215 A | 17-09-96 |
| | | CA 2168347 A | 09-02-95 |
| | | EP 0712301 A | 22-05-96 |
| WO 9503747 A | 09-02-95 | AU 7515594 A | 28-02-95 |
| | | BR 9407170 A | 17-09-96 |
| | | CA 2168789 A | 09-02-95 |
| | | EP 0712297 A | 22-05-96 |
| WO 9626690 A | 06-09-96 | AU 5419496 A | 18-09-96 |